```
 e rosiglitazone
E1            9     ROSIGLIT/BI
E2            9     ROSIGLITAZO/BI
E3            9 --> ROSIGLITAZONE/BI
E4            1     ROSIGLIZ/BI
E5            1     ROSIGLIZOL/BI
E6            1     ROSIGLIZOLE/BI
E7            7     ROSIL/BI
E8            1     ROSIM/BI
E9            1     ROSIMOL/BI
E10           2     ROSIMON/BI
E11        1444     ROSIN/BI
E12         370     ROSINA/BI

=> d e3
NO L# DEFINED

=> s e3
L1            9 ROSIGLITAZONE/BI

=> d ;1

L1   ANSWER 1 OF 9  REGISTRY  COPYRIGHT 2008 ACS on STN
RN   403731-62-4  REGISTRY
ED   Entered STN:  03 Apr 2002
CN   2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
     hyl]-, nitrate (1:1)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
     hyl]-, mononitrate (9CI)
OTHER NAMES:
CN   Rosiglitazone nitrate
MF   C18 H19 N3 O3 S . H N O3
SR   CA
LC   STN Files:   CA, CAPLUS, USPAT2, USPATFULL

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     CRN  122320-73-4
     CMF  C18 H19 N3 O3 S
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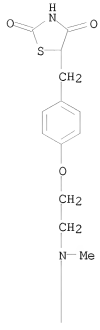

CM 2

CRN 7697-37-2
CMF H N O3

3 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> e "coenzyme Q10"

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E1            1     COENZILE/BI
E2        15824     COENZYME/BI
E3            0 --> COENZYME Q10/BI
E4            2     COENZYMEA/BI
E5            1     COENZYMES/BI
E6            2     COEQ1/BI
E7            5     COER/BI
E8           28     COER0/BI
E9            1     COER0-1O3SM0-1/BI
E10           1     COER0.01HF0.35SBTI0.3ZR0.35/BI
E11           1     COER0.03HF0.34SBTI0.29ZR0.34/BI
E12           1     COER0.05O2.8SR0.95/BI

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 8.07       8.28

FILE 'CAPLUS' ENTERED AT 23:23:04 ON 27 JUN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 27 Jun 2008  VOL 149 ISS 1
FILE LAST UPDATED: 26 Jun 2008  (20080626/ED)

Caplus now includes complete International Patent Classification (IPC)
reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/legal/infopolicy.html

=> s L1 and antioxidant
          2741 L1
        132221 ANTIOXIDANT
        118752 ANTIOXIDANTS
        169354 ANTIOXIDANT
                (ANTIOXIDANT OR ANTIOXIDANTS)
L2          92 L1 AND ANTIOXIDANT

=> s L2 and "coenzyme Q10"
         32005 "COENZYME"
          6589 "COENZYMES"
         35321 "COENZYME"
                ("COENZYME" OR "COENZYMES")
          6640 "Q10"
          3636 "COENZYME Q10"
                 ("COENZYME"(W)"Q10")
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L3            4 L2 AND "COENZYME Q10"

=> d L3 1-4 ibib ab

L3   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:1215859  CAPLUS
DOCUMENT NUMBER:          147:502369
TITLE:                    Fused heterocyclic-substituted dihydroxyheptenoic acid
                          as HMG-CoA reductase inhibitors and their preparation,
                          pharmaceutical compositions and use in the treatment
                          of diseases
INVENTOR(S):              Stein, Philip D.; Seitz, Steven P.; Carini, David J.;
                          Shi, Yan; Robl, Jeffrey A.; Markwalder, Jay A.; He,
                          Chunhong
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Company, USA
SOURCE:                   U.S. Pat. Appl. Publ., 248pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     US 20070249583        A1    20071025    US 2007-789335          20070424
PRIORITY APPLN. INFO.:                       US 2006-794733P     P   20060425
OTHER SOURCE(S):          MARPAT 147:502369
AB   Compds. of formula I are HMG-CoA reductase inhibitors and thus are active
     in inhibiting cholesterol biosynthesis, modulating blood serum lipids, for
     example, lowering LDL cholesterol and/or increasing HDL cholesterol, and
     treating hyperlipidemia and dyslipidemia, hypercholesterolemia,
     hypertriglyceridemia and atherosclerosis.  A method for treating the above
     diseases employing the above compds. is also provided.  Compds. of formula
     I wherein A is CH(OH)CH2CR1(OH)CH2CO2R2 and (un)substituted
     hydroxy(oxo)tetrahydropyranyl; R1 and R2 are independently H and lower
     alkyl; B is (un)substituted benzocycloheptapyridinyl, (un)substituted
     benzopyridinoxazepinyl, (un)substituted benzopyridinoxazepinyl, etc.; and
     their pharmaceutically acceptable salts, esters, prodrugs esters, and
     stereoisomers thereof, are claimed.  Example compound II was prepared by a
     multistep procedure (procedure given).  All the invention compds. were
     evaluated for their HMG-CoA reductase inhibitory activity.

L3   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2004:309876  CAPLUS
DOCUMENT NUMBER:          140:309427
TITLE:                    Pharmaceutical compositions containing synergistic
                          combination of a peroxisome-proliferation activated
                          receptor ligand and an antioxidant agent
INVENTOR(S):              Casteilla, Louis; Penicaud, Luc; Dacquet, Catherine;
                          Renard, Pierre
PATENT ASSIGNEE(S):       Les Laboratoires Servier, Fr.; Centre National de la
                          Recherche Scientifique CNRS
SOURCE:                   Fr. Demande, 15 pp.
                          CODEN: FRXXBL
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
```

FR 2845602	A1	20040416	FR 2002-12646		20021011
CA 2501964	A1	20040422	CA 2003-2501964		20031010
WO 2004032967	A1	20040422	WO 2003-FR2986		20031010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003299772	A1	20040504	AU 2003-299772		20031010
EP 1549348	A1	20050706	EP 2003-807889		20031010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003014539	A	20050726	BR 2003-14539		20031010
CN 1703244	A	20051130	CN 2003-80101191		20031010
JP 2006505548	T	20060216	JP 2004-542579		20031010
EP 1815858	A2	20070808	EP 2007-75195		20031010
EP 1815858	A3	20071219			
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR, AL, LT, LV, MK					
US 20060002911	A1	20060105	US 2005-530771		20050407
MX 2005PA03893	A	20050803	MX 2005-PA3893		20050411
NO 2005002231	A	20050506	NO 2005-2231		20050506
PRIORITY APPLN. INFO.:			FR 2002-12646	A	20021011
			EP 2003-807889	A3	20031010
			WO 2003-FR2986	W	20031010

AB The title compns. are claimed. Synergistic efficacy of rosiglitazone (I) and coenzyme Q10 (II) in treating type II diabetic guinea pigs is shown. A tablet contained I 300, II 100, wheat starch 2000, maize starch 2000, lactose 3000, magnesium stearate 200, silica 100, and hydroxypropyl cellulose 200 g.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:392237 CAPLUS
DOCUMENT NUMBER: 136:401651
TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20020061901	A1	20020523	US 2001-8154		20011204
US 6620821	B2	20030916			
US 20020028826	A1	20020307	US 2001-875218		20010606
US 20040024216	A1	20040205	US 2003-602753		20030624
PRIORITY APPLN. INFO.:			US 2000-211594P	P	20000615
			US 2001-875218	A2	20010606

OTHER SOURCE(S): MARPAT 136:401651

AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl; R4 = H, halo, CF3, OH, alkyl, alkoxy, CO2H, (un)substituted NH2, cyano, (un)substituted CONH2, etc.; R7 = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Prepns. of several compds. are described. For instance, a multistep synthesis of fused pyridine derivative II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:396644 CAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248363	B1	20010619	US 1999-447690	19991123
CA 2391923	A1	20010531	CA 2000-2391923	20001122
EP 1233756	A1	20020828	EP 2000-980761	20001122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T	20030527	JP 2001-539423	20001122
PRIORITY APPLN. INFO.:			US 1999-447690 A	19991123
			WO 2000-US32255 W	20001122

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained

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     therein or sep. administered.  In one embodiment, the solid pharmaceutical
     composition includes a solid carrier, the solid carrier including a substrate
     and an encapsulation coat on the substrate.  The encapsulation coat can
     include different combinations of pharmaceutical active ingredients,
     hydrophilic surfactant, lipophilic surfactants and triglycerides.  In
     another embodiment, the solid pharmaceutical composition includes a solid
     carrier, the solid carrier being formed of different combinations of
     pharmaceutical active ingredients, hydrophilic surfactants, lipophilic
     surfactants and triglycerides.  The compns. of the present invention can
     be used for improved delivery of hydrophilic or hydrophobic pharmaceutical
     active ingredients, such as drugs, nutritionals, cosmeceuticals and
     diagnostic agents.  A composition contained glyburide 1, PEG 40 stearate 33,
     glycerol monolaurate 17, and nonpareil seed 80 g.
REFERENCE COUNT:         4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 23:21:40 ON 27 JUN 2008)

     FILE 'REGISTRY' ENTERED AT 23:21:50 ON 27 JUN 2008
                E ROSIGLITAZONE
L1             9 S E3
                E "COENZYME Q10"

     FILE 'CAPLUS' ENTERED AT 23:23:04 ON 27 JUN 2008
L2            92 S L1 AND ANTIOXIDANT
L3             4 S L2 AND "COENZYME Q10"

=> S L2 AND 1960<=PY<=2003
      21227234 1960<=PY<=2003
L4           22 L2 AND 1960<=PY<=2003

=> dup rem L4
PROCESSING COMPLETED FOR L4
L5            22 DUP REM L4 (0 DUPLICATES REMOVED)

=> d L5 1-22 ibib ab

L5   ANSWER 1 OF 22  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:620087  CAPLUS
DOCUMENT NUMBER:          147:16717
TITLE:                    Progenitor endothelial cell capturing with a
                          drug-eluting implantable medical device
INVENTOR(S):              Cottone, Robert John, Jr.; Rowland, Stephen M.;
                          Parker, Sherry
PATENT ASSIGNEE(S):       Orbusneich Medical, Inc., USA
SOURCE:                   U.S. Pat. Appl. Publ., 47pp., Cont.-in-part of U.S.
                          Ser. No. 76,731.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   13
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     US 20070129789       A1    20070607    US 2006-561730         20061120
     US 20020049495       A1    20020425    US 2001-808867         20010315 <--
     US 7037332           B2    20060502
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US 20030229393	A1	20031211	US 2003-360567	20030206	<--
WO 2003099169	A1	20031204	WO 2003-US15811	20030520	<--
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003241515	A1	20031212	AU 2003-241515	20030520	<--
US 20040039441	A1	20040226	US 2003-442669	20030520	
CN 1655738	A	20050817	CN 2003-811531	20030520	
JP 2005525911	T	20050902	JP 2004-506697	20030520	
US 20050271701	A1	20051208	US 2005-76731	20050310	
US 20070134290	A1	20070614	US 2006-494801	20060726	
US 20070156232	A1	20070705	US 2006-562931	20061122	
PRIORITY APPLN. INFO.:			US 2000-189674P	P 20000315	
			US 2000-201789P	P 20000504	
			US 2001-808867	A2 20010315	
			US 2002-354680P	P 20020206	
			US 2002-382095P	P 20020520	
			US 2003-360567	A2 20030206	
			US 2003-442669	B2 20030520	
			US 2004-551978P	P 20040310	
			US 2005-76731	A2 20050310	
			US 2006-822451P	P 20060815	
			WO 2003-US15811	W 20030520	
			US 2004-832106	A1 20040426	

AB A medical device for implantation into vessels or luminal structures within the body is provided, which stimulates pos. blood vessel remodeling. The medical device, such as a stent and a synthetic graft, is coated with a pharmaceutical composition consisting of a controlled-release matrix and one or more pharmaceutical substances for direct delivery of drugs to surrounding tissues. The coating on the medical device further comprises a ligand such as a peptide, an antibody or a small mol. for capturing progenitor endothelial cells in the blood contacting surface of the device for restoring an endothelium at the site of injury. In particular, the drug-coated stents are for use, for example, in balloon angioplasty procedures for preventing or inhibiting restenosis.

L5 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2005:1294050 CAPLUS
DOCUMENT NUMBER:	144:40902
TITLE:	Progenitor endothelial cell capturing with a drug eluting implantable medical device
INVENTOR(S):	Cottone, Robert J., Jr.; Rowland, Stephen M.; Davis, Horace R.; Kutryk, Michael J. B.
PATENT ASSIGNEE(S):	Orbus Medical Technologies, Inc., USA
SOURCE:	U.S. Pat. Appl. Publ., 38 pp., Cont.-in-part of U.S. Ser. No. 442,669. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	13
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 20050271701	A1	20051208	US 2005-76731		20050310
US 20020049495	A1	20020425	US 2001-808867		20010315 <--
US 7037332	B2	20060502			
US 20030229393	A1	20031211	US 2003-360567		20030206 <--
WO 2003099169	A1	20031204	WO 2003-US15811		20030520 <--

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003241515	A1	20031212	AU 2003-241515		20030520 <--
US 20040039441	A1	20040226	US 2003-442669		20030520
CN 1655738	A	20050817	CN 2003-811531		20030520
JP 2005525911	T	20050902	JP 2004-506697		20030520
US 20070134290	A1	20070614	US 2006-494801		20060726
US 20070128723	A1	20070607	US 2006-560352		20061115
US 20070141107	A1	20070621	US 2006-560356		20061115
US 20070129789	A1	20070607	US 2006-561730		20061120
US 20070156232	A1	20070705	US 2006-562931		20061122
PRIORITY APPLN. INFO.:			US 2000-189674P	P	20000315
			US 2000-201789P	P	20000504
			US 2001-808867	A2	20010315
			US 2002-354680P	P	20020206
			US 2002-382095P	P	20020520
			US 2003-360567	A2	20030206
			US 2003-442669	A2	20030520
			US 2004-551978P	P	20040310
			WO 2003-US15811	W	20030520
			US 2004-832106	A1	20040426
			US 2005-76731	A2	20050310
			US 2005-736920P	P	20051115
			US 2006-822451P	P	20060815
			US 2006-822471P	P	20060815

AB A medical device for implantation into vessels or luminal structures within the body is provided. The medical device, such as a stent and a synthetic graft, is coated with a pharmaceutical composition consisting of a controlled-release matrix and one or more pharmaceutical substances for direct delivery of drugs to surrounding tissues. The coating on the medical device further comprises a ligand such as an antibody or a small mol. for capturing progenitor endothelial cells in the blood contacting surface of the device for restoring an endothelium at the site of injury. In particular, the drug-coated stents are for use, for example, in balloon angioplasty procedures for preventing or inhibiting restenosis.

L5 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2004:392331 CAPLUS
DOCUMENT NUMBER:	140:406798
TITLE:	Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors
INVENTOR(S):	Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S):	Bristol-Myers Squibb Company, USA
SOURCE:	U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 875,155, abandoned. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 20040092573	A1	20040513	US 2003-602752		20030624	
US 6812345	B2	20041102				
US 20020013334	A1	20020131	US 2001-875155		20010606	<--
PRIORITY APPLN. INFO.:			US 2000-211595P	P	20000615	
			US 2001-875155	B2	20010606	

OTHER SOURCE(S): MARPAT 140:406798
AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:157498 CAPLUS
DOCUMENT NUMBER: 140:199313
TITLE: Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors
INVENTOR(S): Daisy, Joe
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 1391460	A1	20040225	EP 2003-20676		20000918	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY						
EP 1088824	A2	20010404	EP 2000-308131		20000918	<--
EP 1088824	A3	20010627				
EP 1088824	B1	20040107				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO						
US 20020183369	A1	20021205	US 2002-117370		20020405	<--
US 6576653	B2	20030610				
US 20030195361	A1	20031016	US 2003-367002		20030214	<--
US 6828343	B2	20041207				
PRIORITY APPLN. INFO.:			US 1999-157148P	P	19990930	
			EP 2000-308131	A3	20000918	
			US 2000-670759	A3	20000927	
			US 2002-117370	A3	20020405	

OTHER SOURCE(S): MARPAT 140:199313
AB Title compds. [I; Q = substituted aryl, heteroaryl; Z, X = C, CH, CH2, N, O, S; X1 = NRa, CH2, O , S; dotted lines = bond, null; both dotted lines are not simultaneously bonds; R1 = H, halo, alkoxy, alkylthio, alkyl, CF3, NH2, alkylamino, dialkylamino, NO2, CN, CO2H, carboxyalkyl, alkenyl,

alkynyl; Ra, Rb = H, alkyl; Y = CH(OH), null; R2R3 = atoms to form a 5-6 membered ring containing 0-3 heteroatoms and 0-2 double bonds; R4 = COA; A = NRdRd, NRaCH2CH2ORa, N-heterocyclyl; Rd = H, alkyl, alkoxy, aryl, (substituted) aryl, heteroaryl; Rc = H, CO2Ra, ORa, SRa, NRaRa; n = 1-3], were prepared for treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, or tissue ischemia (no data). Thus, 6H-thieno[2,3-b]pyrrole-5-carboxylic acid and (3S)-amino-1-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-4-phenylbutan-1-one were coupled using 4-(dimethylamino)pyridine, 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in CH2Cl2/DMF to give 6H-thieno[2,3-b]pyrrole-5-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxopropyl]amide.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:590998 CAPLUS
DOCUMENT NUMBER: 139:128037
TITLE: Use of acetylcholine esterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061648	A1	20030731	WO 2003-CA78	20030127 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030235609	A1	20031225	US 2003-350478	20030124 <--
CA 2514088	A1	20030731	CA 2003-2514088	20030127 <--
EP 1471905	A1	20041103	EP 2003-700275	20030127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005519906	T	20050707	JP 2003-561592	20030127
AU 2003201578	B2	20080306	AU 2003-201578	20030127
US 20050049293	A1	20050303	US 2004-502066	20041027
PRIORITY APPLN. INFO.:			US 2002-350958P	P 20020125
			WO 2003-CA78	W 20030127

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:590992 CAPLUS
DOCUMENT NUMBER: 139:128035
TITLE: Use of phosphodiesterase antagonists to treat insulin resistance
INVENTOR(S): Lautt, Wayne W.; Macedo, Paula
PATENT ASSIGNEE(S): Diamedica Inc., Can.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061638	A2	20030731	WO 2003-CA77	20030127 <--
WO 2003061638	A3	20031002		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20030181461	A1	20030925	US 2003-350070	20030124 <--
CA 2514081	A1	20030731	CA 2003-2514081	20030127 <--
EP 1471897	A2	20041103	EP 2003-700274	20030127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2003201577	B2	20071004	AU 2003-201577	20030127
US 20050119272	A1	20050602	US 2005-502119	20050112
PRIORITY APPLN. INFO.:			US 2002-350954P P	20020125
			WO 2003-CA77 W	20030127

AB There is provided the use of a phosphodiesterase antagonist to reduce insulin resistance, and to amplify the effect of nitric oxide on skeletal muscle insulin-mediated glucose uptake in a mammal. In some instances, the antagonist is targeted to the liver. In some instances, the insulin resistance is hepatic insulin sensitizing substance ('HISS') dependant insulin resistance.

L5 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:909079 CAPLUS
DOCUMENT NUMBER: 141:17148
TITLE: Antioxidative, Antinitrative, and Vasculoprotective Effects of a Peroxisome Proliferator-Activated Receptor-γ Agonist in Hypercholesterolemia
AUTHOR(S): Tao, Ling; Liu, Hui-Rong; Gao, Erhe; Teng, Zhi-Ping; Lopez, Bernard L.; Christopher, Theodore A.; Ma, Xin-Liang; Batinic-Haberle, Ines; Willette, Robert N.; Ohlstein, Eliot H.; Yue, Tian-Li
CORPORATE SOURCE: Department of Emergency Medicine, Thomas Jefferson University, Philadelphia, PA, USA
SOURCE: Circulation (2003), 108(22), 2805-2811
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Peroxisome proliferator-activated receptor (PPAR) signaling

pathways have been reported to exert anti-inflammatory effects and attenuate atherosclerosis formation. However, the mechanisms responsible for their anti-inflammatory and antiatherosclerotic effects remain largely unknown. The present study tested the hypothesis that a PPARγ agonist may exert significant endothelial protection by antioxidative and antinitrative effects. Methods and Results: Male New Zealand White rabbits were randomized to receive a normal (control) or a high-cholesterol diet and treated with vehicle or rosiglitazone (a PPARγ agonist) 3 mg · kg-1 · d-1 for 5 wk beginning 3 wk after the high-cholesterol diet. At the end of 8 wk of a high-cholesterol diet, the rabbits were killed, and the carotid arteries were isolated. Bioactive nitric oxide was determined functionally (endothelium-dependent vasodilatation) and biochem. (the phosphorylation of vasodilator-stimulated phosphoprotein, or P-VASP). Vascular superoxide production, PPARγ, gp91phox, and inducible nitric oxide synthase (iNOS) expression, and vascular ONOO- formation were determined Hypercholesterolemia caused severe endothelial dysfunction and reduced P-VASP, despite a marked increase in iNOS expression and total NOx production Treatment with rosiglitazone enhanced PPARγ expression, improved endothelium-dependent vasodilatation, preserved P-VASP, suppressed gp91phox and iNOS expression, reduced superoxide and total NOx production, and inhibited nitrotyrosine formation. Conclusions: The PPARγ agonist rosiglitazone exerted a significant vascular protective effect in hypercholesterolemic rabbits, most likely by attenuation of oxidative and nitrative stresses. The endothelial protective effects of PPARγ agonists may reduce leukocyte accumulation in vascular walls and contribute to their antiatherosclerotic effect.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:637483 CAPLUS
DOCUMENT NUMBER: 137:185311
TITLE: Preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders
INVENTOR(S): Adams, Alan D.; Jones, A. Brian; Berger, Joel P.; Dropinski, James F.; Elbrecht, Alexander; Liu, Kun; Macnaul, Karen Lamb; Shi, Guo-qiang; Von, Langen Derek J.; Zhou, Gaochao
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064094	A2	20020822	WO 2002-US4680	20020205 <--
WO 2002064094	A3	20030612		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2437118		A1	20020822	CA 2002-2437118		20020205 <--
AU 2002251978		A1	20020828	AU 2002-251978		20020205 <--
AU 2002251978		B2	20070719			
EP 1366012		A2	20031203	EP 2002-721022		20020205 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR						
JP 2004521124		T	20040715	JP 2002-563891		20020205
US 20040092596		A1	20040513	US 2003-470954		20030730
US 7091230		B2	20060815			
US 20060122242		A1	20060608	US 2006-334152		20060118
PRIORITY APPLN. INFO.:				US 2001-267809P	P	20010209
				WO 2002-US4680	W	20020205
				US 2003-470954	A3	20030730

OTHER SOURCE(S): MARPAT 137:185311

AB Title compds. I [R1 = halo, alkyl, alkoxy; R2 = alkyl, alicyclic; R3 = alkyl, aryl, alicyclic, heterocycle, etc.; R4 = H, OH, alkoxy, aryloxy, halo or R3-4 may be joined together to yield 5- or 6-membered heterocycle; R5 = H, halo; R6 = H, halo, CH3, CF3; Ar1 = Ph, thienyl, thiazolyl, oxazolyl, pyridyl; X = O, S; Z = COOH, tetrazole, carboxamide] were prepared For instance, 2,4-dipropylresorcinol was converted to 2,4-dihydroxy-3,5-dipropyl-α,α,α-trifluoroacetophenone (CH2Cl2, TFAA, AlCl3) and subsequently treated with i. hydroxylamine•HCl, MeOH, reflux; ii. Ac2O; iii. pyridine, reflux which afforded 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. The benzisoxazole was reacted with Me 2-bromo-2-phenylacetate (DMF, Cs2CO3) and the product saponified to give II. I are potent agonists of the peroxisome proliferator activated receptor and are useful in the treatment of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR-α and/or PPAR-γ mediated diseases.

L5 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:594636 CAPLUS
DOCUMENT NUMBER: 137:135097
TITLE: Acyl sulfamides for treatment of obesity, diabetes and lipid disorders
INVENTOR(S): Jones, A. Brian; Acton, John J., III
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060388	A2	20020808	WO 2002-US3119	20020125 <--
WO 2002060388	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2434491	A1	20020808	CA 2002-2434491	20020125 <--
AU 2002240235	A1	20020812	AU 2002-240235	20020125 <--

AU 2002240235 B2 20060706
EP 1357908 A2 20031105 EP 2002-706128 20020125 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004521119 T 20040715 JP 2002-560584 20020125
US 20040073037 A1 20040415 US 2003-470483 20030729
US 6852738 B2 20050208
PRIORITY APPLN. INFO.: US 2001-264955P P 20010130
WO 2002-US3119 W 20020125
OTHER SOURCE(S): MARPAT 137:135097

AB A class of acyl sulfamides comprises compds. that are potent ligands for PPARγ receptors and generally have antagonist or partial agonist activity. The compds. may be useful in the treatment, control or prevention of obesity, non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, vascular restenosis, inflammation, and other PPARγ receptor-mediated diseases, disorders and conditions, alone or in combination with one or more other compds. Other compds. are selected from insulin sensitizers, insulin or insulin mimetics, sulfonylureas, α-glucosidase inhibitors, cholesterol lowering agents, PPARδ agonists, antiobesity compds., an ileal bile acid transporter inhibitor, and agents intended for use in inflammatory conditions such as aspirin, nonsteroidal anti-inflammatory drugs, glucocorticoids, azulfidine, and cyclooxygenase-2 selective inhibitors.

L5 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:171676 CAPLUS
DOCUMENT NUMBER: 136:205464
TITLE: Compositions for the treatment of hypertriglyceridemia
INVENTOR(S): Surette, Marc E.
PATENT ASSIGNEE(S): Pilot Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017906	A1	20020307	WO 2001-US26053	20010821 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20020044981	A1	20020418	US 2001-826437	20010405 <--
US 6667064	B2	20031223		
CA 2420835	A1	20020307	CA 2001-2420835	20010821 <--
AU 2001086576	A	20020313	AU 2001-86576	20010821 <--
EP 1313465	A1	20030528	EP 2001-966032	20010821 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004507498	T	20040311	JP 2002-522880	20010821
NZ 524376	A	20041126	NZ 2001-524376	20010821
AU 2001286576	B2	20061207	AU 2001-286576	20010821
ZA 2003001525	A	20040416	ZA 2003-1525	20030225

MX 2003PA01796	A	20050620	MX 2003-PA1796		20030228
US 20040058024	A1	20040325	US 2003-667529		20030922
US 7195914	B2	20070327			
PRIORITY APPLN. INFO.:			US 2000-228930P	P	20000830
			US 2001-826437	A	20010405
			WO 2001-US26053	W	20010821

AB A polyunsatd. fatty acid-containing composition for treating hypertriglyceridemia is provided. Thus, a composition contained water 49.28, ascorbyl palmitate 0.2, sorbic acid 0.16, sucrose 5, glycerin 5, Echium plantagineum seed oil 35, atorvastatin 5, and dye 0.05 g.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:575765 CAPLUS

DOCUMENT NUMBER: 137:140435

TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of diabetes and lipid disorders, and their preparation, pharmaceutical compositions, and use

INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020103242	A1	20020801	US 2001-21667	20011029 <--
US 6713508	B2	20040330		
CA 2427610	A1	20020808	CA 2001-2427610	20011026 <--
WO 2002060434	A2	20020808	WO 2001-US49501	20011026 <--
WO 2002060434	A3	20030619		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002248221	A1	20020812	AU 2002-248221	20011026 <--
AU 2002248221	B2	20060817		
EP 1347755	A2	20031001	EP 2001-997102	20011026 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517938	T	20040617	JP 2002-560626	20011026
PRIORITY APPLN. INFO.:			US 2000-244698P	P 20001031
			WO 2001-US49501	W 20011026

OTHER SOURCE(S): MARPAT 137:140435

AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes

mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms (un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their preparation is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alkaline hydrolysis (100%), to give title compound II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a number of specific drugs, is claimed.

L5 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:540258 CAPLUS
DOCUMENT NUMBER: 137:109267
TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 20020094977	A1	20020718	US 2001-7407		20011204	<--
US 6627636	B2	20030930				
US 20020013334	A1	20020131	US 2001-875155		20010606	<--
			US 2000-211595P	P	20000615	
			US 2001-875155	A2	20010606	

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 137:109267
AB Title compds. I [X = O, S, SO, SO2, NR7; Z = HOCHCH2CH(OH)CH2CO2R3, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H, alkyl, metal ion; R4 = H, halo, CF3, etc.; R7 = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R9, R10 = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDl cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and atherosclerosis (no data). A multistep synthesis of II is reported.

L5 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:392237 CAPLUS

DOCUMENT NUMBER: 136:401651
TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020061901	A1	20020523	US 2001-8154	20011204 <--
US 6620821	B2	20030916		
US 20020028826	A1	20020307	US 2001-875218	20010606 <--
US 20040024216	A1	20040205	US 2003-602753	20030624

PRIORITY APPLN. INFO.: US 2000-211594P P 20000615
US 2001-875218 A2 20010606
US 2001-8154 A3 20011204

OTHER SOURCE(S): MARPAT 136:401651

AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl; R4 = H, halo, CF3, OH, alkyl, alkoxy, CO2H, (un)substituted NH2, cyano, (un)substituted CONH2, etc.; R7 = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Prepns. of several compds. are described. For instance, a multistep synthesis of fused pyridine derivative II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

L5 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:963304 CAPLUS
DOCUMENT NUMBER: 138:232836
TITLE: Identification of a functional peroxisome proliferator-activated receptor response element in the rat catalase promoter
AUTHOR(S): Girnun, Geoffrey D.; Domann, Frederick E.; Moore, Steven A.; Robbins, Mike E. C.
CORPORATE SOURCE: Free Radical and Radiation Biology Program, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Molecular Endocrinology (2002), 16(12), 2793-2801
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisomal proliferator-activated receptor (PPAR)γ has been shown to decrease the inflammatory response via transrepression of proinflammatory transcription factors. However, the identity of PPARγ responsive genes that decrease the inflammatory response has remained elusive. Because generation of the reactive oxygen species hydrogen peroxide (H2O2) plays a role in the inflammatory process and activation of proinflammatory transcription factors, the authors wanted to determine whether the antioxidant enzyme catalase might be a PPARγ target gene. The authors identified a putative PPAR response element (PPRE) containing the canonical direct repeat 1 motif, AGGTGA-A-AGTTGA, in the rat catalase promoter. In vitro translated PPARγ and retinoic X receptor-α proteins were able to bind to the catalase PPRE. Promoter deletion anal. revealed that the PPRE was functional, and a heterologous promoter construct containing a multimerized catalase PPRE demonstrated that the PPRE was necessary and sufficient for PPARγ-mediated activation. Treatment of microvascular endothelial cells with PPARγ ligands led to increases in catalase mRNA and activity. These results demonstrate that PPARγ can alter catalase expression; this occurs via a PPRE in the rat catalase promoter. Thus, in addition to transrepression of proinflammatory transcription factors, PPARγ may also be modulating catalase expression, and hence down-regulating the inflammatory response via scavenging of reactive oxygen species.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:12135 CAPLUS

DOCUMENT NUMBER: 136:226607

TITLE: Unique ability of troglitazone to up-regulate peroxisome proliferator-activated receptor-γ expression in hepatocytes

AUTHOR(S): Davies, Gerald F.; McFie, Pamela J.; Khandelwal, Ramji L.; Roesler, William J.

CORPORATE SOURCE: Department of Biochemistry, University of Saskatchewan, Saskatoon, SK, Can.

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 300(1), 72-77
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferator-activated receptor-γ (PPAR-γ) is a nuclear receptor that is activated by the binding of an appropriate ligand. Several studies have demonstrated that certain ligands can also induce the expression of PPAR-γ. In the present study, we examined the mechanism whereby this induction occurs by specifically addressing whether potentiation of the transactivation function of PPAR-γ per se leads to induction of expression. We observed that thiazolidinediones, a group of insulin-sensitizing drugs, had differential effects, with troglitazone inducing protein levels of PPAR-γ, while rosiglitazone, englitazone, and ciglitazone were without effect. Similarly, the prostaglandin metabolite 15-deoxy-Δ12,14-prostaglandin J2 and the potent synthetic ligand GW1929 (N-(2-benzoyl phenyl)-L-tyrosine) also had no effect, as did ligands for other isoforms of PPAR. Since troglitazone has antioxidant properties, we also examined the effect of α-tocopherol and observed that it induced PPAR-γ expression in a dose-dependent fashion. Finally, we found that mice fed troglitazone as a dietary admixt. displayed an up-regulation of hepatic PPAR-γ mRNA

and protein, indicating that the mechanism of action is at the level of gene expression and not protein stability. These data indicate that (1) up-regulation of the transactivation function of PPAR-γ does not alone account for the induction of expression of PPAR-γ by troglitazone, and (2) an antioxidant-related mechanism may be involved.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:617987 CAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400021	A1	20010823	CA 2001-2400021	20010214 <--
AU 2001038214	A5	20010827	AU 2001-38214	20010214 <--
AU 784722	B2	20060601		
EP 1259494	A1	20021127	EP 2001-910624	20010214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523336	T	20030805	JP 2001-560192	20010214 <--
PRIORITY APPLN. INFO.:			US 2000-183593P	P 20000218
			WO 2001-US4636	W 20010214

OTHER SOURCE(S): MARPAT 135:180757
AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me α-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by saponification, afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) α and/or γ and are

useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPARα and/or γ mediated diseases, disorders, and conditions (no data).
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:396644 CAPLUS
DOCUMENT NUMBER: 135:24671
TITLE: Solid carriers for improved delivery of active ingredients in pharmaceutical compositions
INVENTOR(S): Patel, Manesh V.; Chen, Feng-jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037808	A1	20010531	WO 2000-US32255	20001122 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6248363	B1	20010619	US 1999-447690	19991123 <--
CA 2391923	A1	20010531	CA 2000-2391923	20001122 <--
EP 1233756	A1	20020828	EP 2000-980761	20001122 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517470	T	20030527	JP 2001-539423	20001122 <--
PRIORITY APPLN. INFO.:			US 1999-447690 A	19991123
			WO 2000-US32255 W	20001122

AB The present invention provides solid pharmaceutical compns. for improved delivery of a wide variety of pharmaceutical active ingredients contained therein or sep. administered. In one embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate. The encapsulation coat can include different combinations of pharmaceutical active ingredients, hydrophilic surfactant, lipophilic surfactants and triglycerides. In another embodiment, the solid pharmaceutical composition includes a solid carrier, the solid carrier being formed of different combinations of pharmaceutical active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides. The compns. of the present invention can be used for improved delivery of hydrophilic or hydrophobic pharmaceutical active ingredients, such as drugs, nutritionals, cosmeceuticals and diagnostic agents. A composition contained glyburide 1, PEG 40 stearate 33, glycerol monolaurate 17, and nonpareil seed 80 g.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103 <--
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 1999-165398P	P 19991105
	US 2000-196571P	P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L5 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:300514 CAPLUS
DOCUMENT NUMBER: 134:331617
TITLE: Oil-in-water emulsion compositions for polyfunctional active ingredients
INVENTOR(S): Chen, Feng-jing; Patel, Mahesh V.
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028555	A1	20010426	WO 2000-US28835	20001018 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 20020107265	A1	20020808	US 1999-420159	19991018 <--
US 6720001	B2	20040413		

PRIORITY APPLN. INFO.: US 1999-420159 A 19991018

AB Pharmaceutical oil-in-water emulsions for delivery of polyfunctional active ingredients with improved loading capacity, enhanced stability, and reduced irritation and local toxicity are described. Emulsions include an aqueous phase, an oil phase comprising a structured triglyceride, and an emulsifier. The structured triglyceride of the oil phase is substantially free of triglycerides having three medium chain (C6-C12) fatty acid moieties, or a combination of a long chain triglyceride and a polarity-enhancing polarity modifier. The present invention also provides methods of treating an animal with a polyfunctional active ingredient, using dosage forms of the pharmaceutical emulsions. For example, an emulsion was prepared, with cyclosporin A as the polyfunctional active ingredient dissolved in an oil phase including a structured triglyceride (Captex 810D) and a long chain triglyceride (safflower oil). The composition contained (by weight) cyclosporin A 1.0, Captex 810D 5.0, safflower oil 5.0, BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2, glycerol 2.25, EDTA 0.01, and water up to 100%, resp.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:738033 CAPLUS
DOCUMENT NUMBER: 136:95888
TITLE: Inhibition of phosphoenolpyruvate carboxykinase (PEPCK) gene expression by troglitazone: a peroxisome proliferator-activated receptor-γ (PPARγ)-independent, antioxidant -related mechanism
AUTHOR(S): Davies, G. F.; Khandelwal, R. L.; Wu, L.; Juurlink, B. H. J.; Roesler, W. J.
CORPORATE SOURCE: Department of Biochemistry, University of Saskatchewan, Saskatoon, SK, S7N 5E5, Can.
SOURCE: Biochemical Pharmacology (2001), 62(8), 1071-1079
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phosphoenolpyruvate carboxykinase (PEPCK) is the rate-limiting enzyme of gluconeogenesis. Enhanced expression of the PEPCK gene in liver is present in most models of diabetes, and is thought to contribute to the increased hepatic glucose output seen in this disease. Recently, we showed that troglitazone, the first thiazolidinedione (TZD) used clin., inhibits expression of the PEPCK gene in isolated hepatocytes. We have pursued the mol. mechanism whereby troglitazone exerts this inhibition. TZDs are known to bind and activate peroxisome proliferator-activated

receptor-γ (PPARγ), a nuclear receptor, which regulates expression of target genes. Initially, we examined the abilities of three other TZDs (rosiglitazone, englitazone, and ciglitazone) to inhibit expression of the PEPCK gene. Despite the fact that these agents are ligands for PPARγ, they displayed little if any inhibitory activity on the expression of this gene. GW1929 [N-(2-benzoyl phenyl)-l-tyrosine], another potent PPARγ ligand that is unrelated structurally to TZDs, had no inhibitory effect on PEPCK gene expression, while a natural PPARγ ligand, the prostaglandin metabolite 15-PGJ2 (15-deoxy-Δ12,14-prostaglandin J2), displayed only modest inhibitory activity. Treatment of hepatocytes with ligands for other isoforms of PPAR also had no significant effect on PEPCK gene expression. Troglitazone has an α-tocopherol (vitamin E) moiety that is not present in other TZDs, and treatment of hepatocytes with vitamin E led to an inhibition of PEPCK gene expression. These observations support the conclusion that troglitazone inhibits the expression of the PEPCK gene by a PPARγ-independent, antioxidant-related mechanism.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:486785 CAPLUS

DOCUMENT NUMBER: 136:226506

TITLE: Differential effects among thiazolidinediones on the transcription of thromboxane receptor and angiotensin II type 1 receptor genes

AUTHOR(S): Sugawara, Akira; Takeuchi, Kazuhisa; Uruno, Akira; Ikeda, Yukio; Arima, Shuji; Sato, Kazunori; Sudo, Masataka; Taniyama, Yoshihiro; Ito, Sadayoshi; Sato, Kazunori; Kudo, Masataka; Taniyama, Yoshihiro; Ito, Sadayoshi

CORPORATE SOURCE: Division of Nephrology, Endocrinology, and Vascular Medicine, Department of Medicine, Tohoku University Graduate School of Medicine, Sendai, 980-8574, Japan

SOURCE: Hypertension Research (2001), 24(3), 229-233
CODEN: HRESE4; ISSN: 0916-9636

PUBLISHER: Japanese Society of Hypertension

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferator-activated receptor (PPAR)-γ ligands thiazolidinediones (TZDs) have recently been reported to be anti-hypertensive and anti-atherosclerotic. The authors have previously shown that 1 of the TZDs troglitazone significantly suppressed the transcription of both thromboxane receptor (TXR) and angiotensin II type 1 receptor (AT1R) genes in vascular smooth muscle cells (VSMCs) by activating PPAR-γ. In the present study, the authors compared the effects of troglitazone and other TZDs on the transcription of these genes. TXR and AT1R mRNAs in rat VSMCs were determined by semi-quant. RT-PCR. Luciferase chimeric constructs containing either the 989-bp rat TXR gene promoter or the 1,969-bp rat AT1R gene promoter were transiently transfected into VSMCs. The cells were incubated with troglitazone, RS-1455 (a derivative of troglitazone which does not contain the hindered phenol resembling α-tocopherol), pioglitazone, or rosiglitazone for 12 h before harvesting. MRNA expression levels of TXR and AT1R were significantly decreased by troglitazone in contrast to rosiglitazone. TXR gene and AT1R gene transcription was significantly suppressed by troglitazone in a dose-dependent manner, while RS-1455 was less potent. Pioglitazone and rosiglitazone weakly suppressed the transcription of both genes in a manner almost similar to RS-1455. The authors have shown that troglitazone suppresses transcription of both the TXR and AT1R genes more potently than other TZDs. The structure of troglitazone and RS-1455 is

identical except the hindered phenol, which is recently recognized to function as an antioxidant. Moreover, the authors have shown that the potency for activating PPAR-γ is almost identical between troglitazone and RS-1455. The authors therefore speculate that the strong transcriptional suppression of the TXR and AT1R genes by troglitazone may be mediated in part by its antioxidant effect.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:227438 CAPLUS
DOCUMENT NUMBER: 132:231948
TITLE: Thiazolidinediones alone or in combination with other therapeutic agents for tumor therapy
INVENTOR(S): Copland, John Alton, III; Gasic, Slavisa; Urban, Randall; Soloff, Melvyn
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018234	A1	20000406	WO 1998-US20611	19980929 <--
W: CA, JP				
PRIORITY APPLN. INFO.:			WO 1998-US20611	19980929

AB A purpose of the invention is to identify and/or develop nontoxic or low toxic chemotherapeutic regimens to treat cancer. Prototype cells tested are derived from an osteosarcoma from an eleven year girl who died after aggressive chemotherapeutic treatment with adriamycin, vincristine, cytoxan, and aramycin-C. The inventive steps described herein include demonstrating that troglitazone inhibits cell proliferation in human osteosarcoma cells, the presence of functional PPAR-γ in such cells, and the demonstration of the ability of troglitazone to lower the IC50 of other chemotherapeutic agents such as 5-fluorouracil and doxorubicin when administered in combination therewith as regarding cell proliferation.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 23:21:40 ON 27 JUN 2008)

FILE 'REGISTRY' ENTERED AT 23:21:50 ON 27 JUN 2008
E ROSIGLITAZONE
L1 9 S E3
E "COENZYME Q10"

FILE 'CAPLUS' ENTERED AT 23:23:04 ON 27 JUN 2008
L2 92 S L1 AND ANTIOXIDANT
L3 4 S L2 AND "COENZYME Q10"
L4 22 S L2 AND 1960<=PY<=2003
L5 22 DUP REM L4 (0 DUPLICATES REMOVED)

=> s "(PPAR agonists OR "Peroxisome proliferators")"
'"' NOT VALID HERE

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         11349 PPAR
          1429 PPARS
         11521 PPAR
                 (PPAR OR PPARS)
         89772 AGONISTS
           378 PPAR AGONISTS
                 (PPAR(W)AGONISTS)
         21352 "PEROXISOME"
          5224 "PEROXISOMES"
         22454 "PEROXISOME"
                 ("PEROXISOME" OR "PEROXISOMES")
          2264 "PROLIFERATORS"
          2200 "PEROXISOME PROLIFERATORS"
                 ("PEROXISOME"(W)"PROLIFERATORS")
L6        2471 (PPAR AGONISTS OR "PEROXISOME PROLIFERATORS")

=> s ("PPAR agonists" OR "Peroxisome proliferators")
         11349 "PPAR"
          1429 "PPARS"
         11521 "PPAR"
                 ("PPAR" OR "PPARS")
         89772 "AGONISTS"
           378 "PPAR AGONISTS"
                 ("PPAR"(W)"AGONISTS")
         21352 "PEROXISOME"
          5224 "PEROXISOMES"
         22454 "PEROXISOME"
                 ("PEROXISOME" OR "PEROXISOMES")
          2264 "PROLIFERATORS"
          2200 "PEROXISOME PROLIFERATORS"
                 ("PEROXISOME"(W)"PROLIFERATORS")
L7        2471 ("PPAR AGONISTS" OR "PEROXISOME PROLIFERATORS")

=> s L7 and obesity
         50960 OBESITY
            85 OBESITIES
         50963 OBESITY
                 (OBESITY OR OBESITIES)
L8         266 L7 AND OBESITY

=> S L8 AND 1960<=PY<=2003
      21227234 1960<=PY<=2003
L9          24 L8 AND 1960<=PY<=2003

=> d l9 1-24 ibib ab

L9   ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2003:991491  CAPLUS
DOCUMENT NUMBER:          140:27832
TITLE:                    Preparation of triazolyl 11β-hydroxysteroid
                          dehydrogenase-1 inhibitors for the treatment of
                          diabetes, obesity and dyslipidemia
INVENTOR(S):              Olson, Steven H.; Balkovec, James M.; Zhu, Yuping
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 144 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003104208	A1	20031218	WO 2003-US17890	20030606 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2488592	A1	20031218	CA 2003-2488592	20030606 <--
AU 2003251410	A1	20031222	AU 2003-251410	20030606 <--
EP 1532122	A1	20050525	EP 2003-757385	20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1659151	A	20050824	CN 2003-813392	20030606
CN 1990474	A	20070704	CN 2007-10003770	20030606
US 20040048912	A1	20040311	US 2003-457682	20030609
US 6730690	B2	20040504		
US 20040106664	A1	20040603	US 2003-697547	20031030
US 7179802	B2	20070220		
ZA 2004008772	A	20051118	ZA 2004-8772	20041029
PRIORITY APPLN. INFO.:			US 2002-387385P	P 20020610
			CN 2003-813392	A3 20030606
			WO 2003-US17890	W 20030606
			US 2003-457682	A3 20030609

OTHER SOURCE(S): MARPAT 140:27832

AB Title compds. I [A = halo, alkyl, Ph, etc.; B = H, halo, alkyl, S-alkyl, etc. or A, B = taken together are (un)substituted alkylene; R1 = H, OH, halo, alkyl, alkoxy, aryl, etc.; R2 = alkyl, alkoxy, Ph, etc.; R3 = alkyl, alkenyl, thioalkoxy, aryl, heterocyclyl, etc. or R2-3 = taken together fused 5-6-membered alkyl/aryl ring] are prepared For instance, 2,2-diphenylbutanoic acid is converted to the corresponding hydrazide (DMF, Et3N, TFFH, H2NNH2, 0°, 30 min). 8-Methoxy-2,3,4,5,6,7-hexahydroazocine is then reacted with the intermediate (DMF, 120°, overnight) to give II. Example compds. exhibit IC50 < 500 nM for 11β-hydroxysteroid dehydrogenase-1 (11β-HSD1). I are useful for the treatment of diabetes, such as noninsulin-dependent diabetes (NIDDM), hyperglycemia, obesity, insulin resistance, dylsipidemia, hyperlipidemia, hypertension, Syndrome X and other symptoms associated with NIDDM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:950977 CAPLUS
DOCUMENT NUMBER: 140:16514
TITLE: Preparation of (2S)-2-ethyl-3-phenylpropionic acid derivatives as PPAR receptor agonists
INVENTOR(S): Asano, Jun; Isogai, Shigeki; Hori, Wataru
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099766	A1	20031204	WO 2003-JP6515	20030526 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2487450	A1	20031204	CA 2003-2487450	20030526 <--
AU 2003235429	A1	20031212	AU 2003-235429	20030526 <--
EP 1508566	A1	20050223	EP 2003-723401	20030526
EP 1508566	B1	20070718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060084702	A1	20060420	US 2005-515176	20051229
US 7361783	B2	20080422		
PRIORITY APPLN. INFO.:			JP 2002-151700	A 20020527
			WO 2003-JP6515	W 20030526

OTHER SOURCE(S): MARPAT 140:16514

AB The title (2S)-2-ethyl-3-phenylpropionic acid derivs. with general formula of I [wherein R1 = halo or CF3; R2 = H, halo, or CF3; R3 = halo, CF3, or H] and salts thereof are prepared as human peroxisome proliferator-activated receptor (PPAR) agonists. I are effective in lipid depression, arteriosclerotic inhibition, antiobesity, blood sugar depression, etc. For example, the compound II was prepared in a multi-step synthesis. II showed EC50 of 0.0029 μM against human PPARα. II also lowered 28% of total cholesterol and 50% of triglycerides in 14 days in the amount of 0.03 mg/kg/day in dog.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:871110 CAPLUS
DOCUMENT NUMBER: 140:245757
TITLE: Thiazolidine drugs
AUTHOR(S): Yamauchi, Toshimasa; Kadowaki, Takashi
CORPORATE SOURCE: Graduate School of Medicine, University of Tokyo, Japan
SOURCE: Diabetes Frontier (2003), 14(3), 346-353
CODEN: DIFREZ; ISSN: 0915-6593
PUBLISHER: Medikaru Rebyusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review, discussing the action mechanism and clin. pharmacol. of thiazolidine drugs as PPARγ agonists for treatment of obesity, type-2 diabetes, and arteriosclerosis.

L9 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:757811 CAPLUS
DOCUMENT NUMBER: 139:271092
TITLE: Novel metabolic targets and markers
INVENTOR(S): Watkins, Steven M.; Baillie, Rebecca A.
PATENT ASSIGNEE(S): Lipomics Technologies, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078574	A2	20030925	WO 2003-US7242	20030307 <--
WO 2003078574	A3	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2477909	A1	20030925	CA 2003-2477909	20030307 <--
AU 2003225726	A1	20030929	AU 2003-225726	20030307 <--
US 20040024065	A1	20040205	US 2003-383850	20030307
EP 1490076	A2	20041229	EP 2003-744631	20030307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060141550	A1	20060629	US 2005-291272	20051130
US 20060084129	A1	20060420	US 2005-296829	20051206

PRIORITY APPLN. INFO.:		
US 2002-363587P	P	20020311
US 2002-373912P	P	20020419
US 2002-401684P	P	20020806
US 2002-424949P	P	20021108
US 2002-436192P	P	20021224
US 2003-383671	B1	20030307
US 2003-383850	B1	20030307
WO 2003-US7242	W	20030307
US 2003-615966	A1	20030709

AB The present invention is based, in part, on the discovery that certain metabolites or metabolic pathways can be used as diagnostic or therapeutic markers. For example, phosphatidylethanolamine-N-methyltransferase (PEMT) activity and other metabolic activities or markers associated therewith can be used either as markers for diagnosing various conditions or as targets for therapeutic treatment of various disease conditions. In one embodiment, the present invention provides a method for regulating the level of a fatty acid in a system. The method includes decreasing the CDP-choline activity in the system. In still another embodiment, the present invention provides a method for regulating a lipoprotein component ratio in a system. The method includes regulating the PEMT activity in the system whereby regulating the lipoprotein component ratio in the system, wherein the lipoprotein component ratio is selected from the group consisting of cholesterol ester to phosphatidylcholine, cholesterol ester to apoprotein, free cholesterol to apoprotein, and triacylglyceride to phosphatidylcholine. In another embodiment, the present invention provides a method of assessing the d. of a lipoprotein in a system. In yet another embodiment, the present invention provides a method for treating or preventing a cardiovascular or neurol. condition.

L9 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:690468 CAPLUS
DOCUMENT NUMBER: 140:104964
TITLE: Bezafibrate, a peroxisome proliferator-activated receptor (PPAR)-α activator, prevents pancreatic

degeneration in obese and diabetic rats
AUTHOR(S): Jia, Dongmei; Otsuki, Makoto
CORPORATE SOURCE: Third Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan
SOURCE: Pancreas (Hagerstown, MD, United States) (2003), 26(3), 286-291
CODEN: PANCE4; ISSN: 0885-3177
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Damage to the exocrine pancreas has been observed in patients and animals with hyperlipidemia and hyperglycemia. Bezafibrate, a peroxisome proliferator-activated receptor (PPAR)-α activator, has been shown to improve lipid and glucose metabolism, and to interfere with the inflammatory response. The objective of this study was to examine the effects of bezafibrate on exocrine pancreas in hyperlipidemic obese and diabetic Otsuka Long-Evans Tokushima Fatty (OLETF) rats that have no cholecystokinin-1 receptor gene expression. One group of rats (n = 8) received a bezafibrate-rich diet (150 mg/100 g normal chow) from 12 wk of age until 30 wk of age, whereas a control group (n = 8) received standard rat chow. Bezafibrate treatment significantly reduced serum triglyceride, total cholesterol, and free fatty acids levels and significantly increased the pancreatic wet weight (1145 ± 54 vs. 874 ± 33 mg/rat, $p < 0.01$), and protein (169 ± 7 vs. 128 ± 11 mg/pancreas $p < 0.01$) and enzyme contents in the pancreas compared with those in untreated control rats. Immunohistochem. studies of the pancreas showed that expression of proinflammatory cytokines such as tumor necrosis factor-α, interleukin-1β and interleukin-6, and α-smooth muscle actin in bezafibrate-treated rats was greatly suppressed compared with that in the untreated control rats. The histopathol. changes such as vacuolar degeneration and tubular complexes observed in the control rat pancreas were markedly improved in bezafibrate-treated rats. Our results suggest that bezafibrate reduces hyperlipidemia, inhibits pancreatic inflammation, and prevents pancreatic degeneration in obese and diabetic OLETF rats.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:395971 CAPLUS
DOCUMENT NUMBER: 139:207505
TITLE: Combination therapy with PPARγ and PPARα agonists increases glucose-stimulated insulin secretion in db/db mice
AUTHOR(S): Yajima, Ken; Hirose, Hiroshi; Fujita, Haruhisa; Seto, Yoshiko; Fujita, Hiroshi; Ukeda, Kaname; Miyashita, Kiichi; Kawai, Toshihide; Yamamoto, Yukihiro; Ogawa, Takeo; Yamada, Taketo; Saruta, Takao
CORPORATE SOURCE: Department of Internal Medicine, Keio University School of Medicine, Tokyo, 160-8582, Japan
SOURCE: American Journal of Physiology (2003), 284(5, Pt. 1), E966-E971
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although peroxisome proliferator-activated receptor (PPAR)γ agonists ameliorate insulin resistance, they sometimes cause body weight gain, and the effect of PPAR agonists on insulin secretion is unclear. We evaluated the effects of combination therapy with a PPARγ agonist, pioglitazone, and a PPARα agonist, bezafibrate,

and a dual agonist, KRP-297, for 4 wk in male C57BL/6J mice and db/db mice, and we investigated glucose-stimulated insulin secretion (GSIS) by in situ pancreatic perfusion. Body weight gain in db/db mice was less with KRP-297 treatment than with pioglitazone or pioglitazone + bezafibrate treatment. Plasma glucose, insulin, triglyceride, and nonesterified fatty acid levels were elevated in untreated db/db mice compared with untreated C57BL/6J mice, and these parameters were significantly ameliorated in the PPARγ agonist-treated groups. Also, PPARγ agonists ameliorated the diminished GSIS and insulin content, and they preserved insulin and GLUT2 staining in db/db mice. GSIS was further increased by PPARγ and -α agonists. We conclude that combination therapy with PPARγ and PPARα agonists may be more useful with respect to body weight and pancreatic GSIS in type 2 diabetes with obesity.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:270940 CAPLUS
DOCUMENT NUMBER: 139:286120
TITLE: Pharmacology of a selective peroxisome proliferator-activated receptor δ agonist, GW501516, in obese dyslipidemic primates
AUTHOR(S): Oliver, William, Jr.; Sternbach, Dan; Hansen, Barbara; Willson, Timothy
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Medical Science Symposia Series (2002), 18(Peroxisome Proliferator Activated Receptors), 131-134
CODEN: MSSYEI; ISSN: 0928-9550
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To evaluate the therapeutic potential of a PPARδ agonist the authors developed a subtype selective small mol. ligand using combinatorial chemical and structure based drug design. GW501516 is a high affinity ligand in a human PPARδ binding assay with Ki = 1.1 ± 0.1 nM with a >1,000-fold selective for PPARδ over the PPARα and γ subtypes. The obese rhesus is a primate model of human metabolic disease that develops spontaneous adult-onset obesity on standard low fat diets and shows a high risk of developing overt diabetes. The prediabetic state of these primates displays many of the same features of human metabolic syndrome X, including dyslipidemia, insulin resistance, central obesity, hyperinsulinemia, and hypertension. Obese rhesus monkeys received increasing doses of GW501516 (0.1, 0.3, 1, and 3 mg/kg, bid) with each dose administered over a 4-wk period and clin. chemistries examined The results of the study demonstrated that PPARδ agonists are likely to have beneficial effects on the lipid triad of low HDLc, increased proportions of small dense LDLc, and elevated triglycerides through a mechanism that increases cholesterol flux from peripheral tissues. These findings further support the value of PPARδ agonists and GW501516 specifically, as therapeutic agents for decreasing the incidence of cardiovascular disease associated with metabolic syndrome X.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:253373 CAPLUS
DOCUMENT NUMBER: 139:111426
TITLE: PPARα/γ ragaglitazar eliminates fatty liver and enhances insulin action in fat-fed rats in

the absence of hepatomegaly

AUTHOR(S): Ye, Ji-Ming; Iglesias, Miguel A.; Watson, David G.; Ellis, Bronwyn; Wood, Leonie; Jensen, Per Bo; Sorensen, Rikke Veggerby; Larsen, Philip Just; Cooney, Gregory J.; Wassermann, Karsten; Kraegen, Edward W.

CORPORATE SOURCE: Diabetes and Obesity Program, Garvan Institute of Medical Research, Sydney, 2010, Australia

SOURCE: American Journal of Physiology (2003), 284(3, Pt. 1), E531-E540
CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferator-activated receptor (PPAR)α and PPARγ agonists lower lipid accumulation in muscle and liver by different mechanisms. We investigated whether benefits could be achieved on insulin sensitivity and lipid metabolism by the dual PPARα/γ agonist ragaglitazar in high fat-fed rats. Ragaglitazar completely eliminated high-fat feeding-induced liver triglyceride accumulation and visceral adiposity, like the PPARα agonist Wy-14643 but without causing hepatomegaly. In contrast, the PPARγ agonist rosiglitazone only slightly lessened liver triglyceride without affecting visceral adiposity. Compared with rosiglitazone or Wy-14643, ragaglitazar showed a much greater effect (79%, $P < 0.05$) to enhance insulin's suppression of hepatic glucose output. Whereas all three PPAR agonists lowered plasma triglyceride levels and lessened muscle long-chain acyl-CoAs, ragaglitazar and rosiglitazone had greater insulin-sensitizing action in muscle than Wy-14643, associated with a threefold increase in plasma adiponectin levels. There was a significant correlation of lipid content and insulin action in liver and particularly muscle with adiponectin levels ($P < 0.01$). We conclude that the PPARα/γ agonist ragaglitazar has a therapeutic potential for insulin-resistant states as a PPARγ ligand, with possible involvement of adiponectin. Addnl., it can counteract fatty liver, hepatic insulin resistance, and visceral adiposity generally associated with PPARα activation, but without hepatomegaly.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:154391 CAPLUS

DOCUMENT NUMBER: 138:187634

TITLE: Preparation of 2-benzyltetrahydrofuran-2-carboxylic acid derivatives as PPAR agonists for treatment of hyperglycemia, hyperlipemia, and inflammatory diseases

INVENTOR(S): Clark, Richard; Matsuura, Fumiyoshi; Emori, Eita; Shinoda, Masanobu; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Inoue, Takashi; Miyashita, Sadakazu; Hihara, Taro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016265	A1	20030227	WO 2002-JP8325	20020816 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002325535 A1 20030303 AU 2002-325535 20020816 <--

EP 1452521 A1 20040901 EP 2002-758850 20020816

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 20050014833 A1 20050120 US 2004-486396 20040211

US 7371777 B2 20080513

PRIORITY APPLN. INFO.: JP 2001-247540 A 20010817

WO 2002-JP8325 W 20020816

OTHER SOURCE(S): MARPAT 138:187634

AB The title compds. I [wherein m, n, and p = independently 0-4; R1-R6 = independently H, OH, CN, halo, NR7R8, (un)substituted alkyl(thio), alkoxy, HO-alkyl(thio), HO-alkoxy, aminoalkyl(thio), halo-alkyl(thio), halo-alkoxy, alkoxyalkyl(thio), alkoxyalkoxy, cycloalkyl(oxy), cycloalkylalkyloxy, cycloalkylthio, alkenyl(oxy), alkenylthio, alkynyl(oxy), alkynylthio, aryl(oxy), arylthio, alkylaryl(oxy), alkylarylthio, aralkyl(oxy), or aralkylthio; R7 and R8 = independently H, CN, CHO, (un)substituted (amino)alkyl, HO-alkyl, halo-alkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, (alkyl)aryl, aralkyl, acyl, or alkoxy-CO; A1 and A2 = independently a single bond, O, S, SO, SO2, (un)substituted amino, or alkenylenyl; L, M, and T = independently a single bond, (un)substituted alkylenyl, alkenylenyl, or alkynylenyl; W = CO2H; X = a single bond, O, OSO2, SO3, (un)substituted amino(thio)carboxy, (thio)carbamato, (thio)carbamoyloxy, (oxy)amino(thio)carbonyl, (amino)(thio)carbamoyl, aminosulfonyl, or sulfonamido; Y = (un)substituted Ar(Ar); Ar = aromatic ring; ring Z = (un)substituted Ar] and salts, esters, and hydrates thereof are prepared as PPAR (peroxisome proliferator-activated receptor) agonists for the treatment of hyperglycemia, hyperlipemia, and inflammatory diseases. For example, the acid II was prepared in a multi-step synthesis starting from 2-chloro-4-propoxybenzoic acid and the corresponding amine (prepn given) in DMF in the presence of Et3N and di-Et cyanophosphonate. II showed EC50 of 0.013, 0.038, and 0.005 μM against PPAR α, PPAR β, and PPAR γ, resp.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:637640 CAPLUS

DOCUMENT NUMBER: 137:185320

TITLE: PPAR agonists, e.g., 3-[4-[2-[3-(2,4-dimethoxyphenyl)-1-heptylureido]ethyl]phenyl]-2-ethoxypropionic acid and analogs, useful particularly as PPARα agonists, and their pharmaceutical compositions and therapeutic use as hypolipemics, antidiabetics, etc.

INVENTOR(S): Hayward, Cheryl Myers; Perry, David Austen

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064549	A1	20020822	WO 2002-IB45	20020107 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2438551	A1	20020822	CA 2002-2438551	20020107 <--
AU 2002216330	A1	20020828	AU 2002-216330	20020107 <--
EP 1360172	A1	20031112	EP 2002-740089	20020107 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007285	A	20040210	BR 2002-7285	20020107
JP 2004529097	T	20040924	JP 2002-564482	20020107
US 20020165282	A1	20021107	US 2002-76740	20020214 <--
US 6699904	B2	20040302		
MX 2003PA07284	A	20031204	MX 2003-PA7284	20030814 <--
PRIORITY APPLN. INFO.:			US 2001-269058P	P 20010215
			WO 2002-IB45	W 20020107

OTHER SOURCE(S): MARPAT 137:185320

AB Title compds. I and their prodrugs and/or pharmaceutically acceptable salts are claimed [wherein: E = CO, SO2; B = CH2, NH; Z = CO2H, CHO, CH2OH, alkoxycarbonyl, cyano, CONHOH, tetrazolyl, tetrazolylaminocarbonyl, 4,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl, 3-oxo-isoxazolidin-4-ylaminocarbonyl, CONHSO2R4; R1 = H, alkyl, cycloalkyl; R2 = H, cycloalkyl, (un)substituted and/or (un)saturated (hetero)aliphatic chain; R3 = (un)substituted alk(en/yn)yl; R4 = alkyl, amino or its (di)((poly)fluoro)alkyl derivs.; R5, R6 = H, alkyl, cycloalkyl, or cycloalkylalkyl; or R5R6 = atoms to form 3- to 6-membered fully saturated carbocyclic ring; A = H, (di)(alkyl)amino, alkanoylamino, alkoxy, or (un)substituted (un)saturated (bi)(hetero)cyclic ring; W = bond, NH, N-alkyl, alkylamino (sic), or alkylene; or W = CR7R8 where R7R8 = atoms to form 3- to 6-membered fully saturated carbocyclic ring]. The compds. are disclosed as PPAR (peroxisome proliferator-activated receptor) agonists, and particularly as PPARα activators (no data). Also disclosed are pharmaceutical compns. containing I, and the use of I to elevate certain plasma lipid levels, including high d. lipoprotein-cholesterol, and to lower certain other plasma lipid levels, such as LDL-cholesterol and triglycerides, and accordingly to treat diseases which are exacerbated by low levels of HDL cholesterol and/or high levels of LDL-cholesterol and triglycerides, such as atherosclerosis and cardiovascular diseases, in mammals, including humans. Further claimed uses include treatment of obesity, diabetes and related conditions, atherosclerosis, hypertension, inflammation, and thrombosis. The compds. may also be administered in combination with a variety of other enzyme inhibitors. A total of 77 synthetic examples cover production of various I and their intermediates. The (R)- and (S)-enantiomers of approx. 15 compds. are specifically claimed. For instance, [4-(2-heptylaminoethyl)phenyl]methanol (preparation in 3 steps given) underwent a sequence of: (1) N-protection with BOC, (2) O-oxidation with MnO2 to an aldehyde, (3) Wittig type reaction of the latter with Ph2P(:O)CH(OEt)CO2Et, (4) reduction of the resultant acrylate ester to a propionate ester, (5) removal of BOC, (6) carbamoylation with 2,4-dimethoxyphenyl isocyanate, and (7) alkaline hydrolysis of the Me ester, to give title compound II.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:575765 CAPLUS
DOCUMENT NUMBER: 137:140435
TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of diabetes and lipid disorders, and their preparation, pharmaceutical compositions, and use
INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020103242	A1	20020801	US 2001-21667	20011029 <--
US 6713508	B2	20040330		
CA 2427610	A1	20020808	CA 2001-2427610	20011026 <--
WO 2002060434	A2	20020808	WO 2001-US49501	20011026 <--
WO 2002060434	A3	20030619		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002248221	A1	20020812	AU 2002-248221	20011026 <--
AU 2002248221	B2	20060817		
EP 1347755	A2	20031001	EP 2001-997102	20011026 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517938	T	20040617	JP 2002-560626	20011026
PRIORITY APPLN. INFO.:			US 2000-244698P P	20001031
			WO 2001-US49501 W	20011026

OTHER SOURCE(S): MARPAT 137:140435
AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms (un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo,

OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their preparation is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alkaline hydrolysis (100%), to give title compound II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a number of specific drugs, is claimed.

L9 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:449653 CAPLUS
DOCUMENT NUMBER: 137:33307
TITLE: Preparation of phenylalkanoic acid derivatives as peroxisome proliferator activated receptor (PPAR) agonists
INVENTOR(S): Miyachi, Hiroyuki; Murakami, Kouji
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046161	A1	20020613	WO 2001-JP10564	20011204 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2430846	A1	20020613	CA 2001-2430846	20011204 <--
AU 2002022574	A	20020618	AU 2002-22574	20011204 <--
EP 1348698	A1	20031001	EP 2001-999557	20011204 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20050101521	A1	20050512	US 2003-433153	20030530
US 7176204	B2	20070213		

PRIORITY APPLN. INFO.: JP 2000-369370 A 20001205
JP 2001-257390 A 20010828
WO 2001-JP10564 W 20011204

OTHER SOURCE(S): MARPAT 137:33307

AB The title compds. I [R1 = H, alkyl, etc.; R2 = alkoxy; R3 = H, alkyl; A = NHCO, etc.; X = (un)substituted pyridyl, etc.] are prepared I are useful for the treatment of hyperlipidemia, diabetes, etc. For example, 2-[[4-ethoxy-3-[[[4-(2-pyridyloxy)phenyl]carbonylamino]methyl]phenyl]methyl]butyric (II) was prepared The effects of II on PPAR α, PPAR γ, PPAR δ were demonstrated.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:88009 CAPLUS
DOCUMENT NUMBER: 136:227021
TITLE: Dehydroepiandrosterone alters phospholipid profiles in Zucker rat muscle tissue
AUTHOR(S): Abadie, Jude M.; Malcom, Gray T.; Porter, Johnny R.; Svec, Frank
CORPORATE SOURCE: Department of Pathology, Louisiana State University Medical Center, New Orleans, LA, 70112, USA
SOURCE: Lipids (2001), 36(12), 1383-1386
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Insulin-resistant muscle tissue contains low proportions of arachidonic acid (AA), and increased proportions of muscle AA correlate with improved insulin sensitivity. Dehydroepiandrosterone (DHEA) and AA, like the thiazolidinedione drugs that decrease insulin resistance (IR), are peroxisome proliferators. Long-chain fatty acids (FA) have been named the "one true" endogenous ligand for activating the peroxisome proliferator-activator receptor (PPAR), and DHEA has been named a "good candidate" as a naturally occurring indirect activator of PPAR. This study was conducted to determine DHEA's effects on lipid profiles of skeletal and cardiac muscle in lean and obese Zucker rats (ZR), a model of IR, type 2 diabetes mellitus, and obesity. We hypothesize that DHEA may alter long-chain FA profiles in muscle tissue of obese rats such that they more closely resemble that of the lean. In our expts., we employed a DHEA and a pair-fed (PF) group for 12 lean and 12 obese ZR. For 30 d, the diet of the two DHEA groups was supplemented with 0.6% DHEA; PF groups were given the average daily calories consumed by their corresponding treatment group. Hearts and gastrocnemius muscles were assayed for phospholipid (PL), free FA, and triglyceride (TG) FA profiles. The proportion of PL AA was significantly greater in both muscle types of lean compared to obese rats. Hearts from both DHEA groups had greater PL proportions of AA and less oleic (18:1) acid than their PF controls. Likewise, 18:1 proportions were significantly lower in the gastrocnemius; however, AA proportions were not significantly different. Similar phenotypic profile differences were observed in the TG fraction of both muscle types. There were no DHEA-related TG FA profile alterations.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:849125 CAPLUS
DOCUMENT NUMBER: 136:128481
TITLE: Novel agents for managing dyslipidaemia
AUTHOR(S): Best, James D.; Jenkins, Alicia J.
CORPORATE SOURCE: Department of Medicine, St Vincent's Hospital Melbourne, University of Melbourne, Victoria, Australia
SOURCE: Expert Opinion on Investigational Drugs (2001), 10(11), 1901-1911
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. An elevated low-d. lipoprotein (LDL) cholesterol level is a strong predictor of coronary heart disease (CHD) risk. Over the past seven years, equally strong evidence has accumulated that lowering LDL cholesterol with HMG-CoA reductase inhibitors or statins reduces CHD risk and there is now wide-spread use of these agents for the primary and

secondary prevention of CHD. Treatment issues remain regarding the appropriate degree of LDL cholesterol reduction and whether, in people with very high levels, it would be preferable to achieve the LDL cholesterol goal with a powerful statin alone or combined with an agent that lowers LDL cholesterol by a different mechanism. The main focus in the development of novel agents is the patient with low high-d. lipoprotein (HDL) cholesterol, usually associated with hypertriglyceridemia. Already prevalent as a risk factor for CHD, this abnormality has been linked with insulin resistance, which is likely to increase greatly over the next decade, along with increasing obesity and diabetes. Agents that have potent HDL cholesterol raising capacity include cholesteryl ester transfer protein (CETP) inhibitors, retinoid X receptor (RXR) selective agonists, specific peroxisome proliferator-activated receptor (PPAR) agonists and estrogen-like compds. Another area of development involves agents that will lower both cholesterol and triglyceride levels, such as partial inhibitors of microsomal triglyceride transfer protein (MTP) and perhaps squalene synthase inhibitors and agonists of AMP kinase. Future emphasis will be on correcting all lipid abnormalities for the prevention of CHD, not just lowering LDL cholesterol.

REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:617987 CAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400021	A1	20010823	CA 2001-2400021	20010214 <--
AU 2001038214	A5	20010827	AU 2001-38214	20010214 <--
AU 784722	B2	20060601		
EP 1259494	A1	20021127	EP 2001-910624	20010214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523336	T	20030805	JP 2001-560192	20010214 <--

PRIORITY APPLN. INFO.: US 2000-183593P P 20000218
WO 2001-US4636 W 20010214

OTHER SOURCE(S): MARPAT 135:180757

AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me α-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by saponification, afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) α and/or γ and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPARα and/or γ mediated diseases, disorders, and conditions (no data).
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:911076 CAPLUS
DOCUMENT NUMBER: 134:71590
TITLE: Preparation of 5-aryl-2,4-thiazolidinedione and oxazolidinedione derivatives as PPAR agonists
INVENTOR(S): Desai, Ranjit C.; Sahoo, Souyma P.; Bergman, Jeffrey P.; Lombardo, Victoria K.; Metzger, Edward J.; Koyama, Hiroo
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078313	A1	20001228	WO 2000-US16769	20000616 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377246	A1	20001228	CA 2000-2377246	20000616 <--
EP 1194147	A1	20020410	EP 2000-942916	20000616 <--
EP 1194147	B1	20070110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
US 6380191	B1	20020430	US 2000-595840	20000616 <--
JP 2003502370	T	20030121	JP 2001-504376	20000616 <--
AU 770870	B2	20040304	AU 2000-57468	20000616
ES 2277842	T3	20070801	ES 2000-942916	20000616
US 20020037911	A1	20020328	US 2001-990470	20011121 <--

US 6465497 B2 20021015
PRIORITY APPLN. INFO.: US 1999-139929P P 19990618
US 2000-595840 A3 20000616
WO 2000-US16769 W 20000616
OTHER SOURCE(S): MARPAT 134:71590
AB The title compds. (I) [wherein Ar1 = (hetero)arylene optionally substituted with 1-4 groups independently selected from Ra or R; Ar2 = (hetero)aryl substituted with 1-2 R groups and optionally substituted with 1-3 Ra groups; X and Y = independently O, S, NRb, or CH2; Z = O or S; n = 0-3; R = (un)substituted cycloalkyl or (un)substituted heterocycle; Ra = halo, ORb, (hetero)aryl, or (un)substituted alkanoyl, alkyl, alkenyl, or alkynyl; Rb = H, (hetero)aryl, (hetero)arylalkyl, alkanoyl, cycloalkyl, or (un)substituted alkyl, alkenyl, or alkynyl] were prepared as peroxisome proliferator activated receptor (PPAR) agonists. For example, 2-propyl-4-cyclohexylphenol and Et 3-(3-bromopropoxy)mandelate (preparation for starting materials given) were stirred at 40°C for 30 h to give Et 3-(3-(2-propyl-4-cyclohexylphenoxy)propoxy)mandelate. α-Chlorination with thionyl chloride in the presence of pyridine produced the chloro derivative, which was treated with thiourea and NaOAc in EtOH to afford the cycloaddn. product (II). I are useful in the treatment, control, or prevention of diabetes, hyperglycemia, hyperlipidemia (including hypercholesterolemia and hypertriglyceridemia), atherosclerosis, obesity, vascular restenosis, and other PPAR α and/or γ mediated diseases, disorders, and conditions (no data).
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:911075 CAPLUS
DOCUMENT NUMBER: 134:71589
TITLE: Preparation of 5-(halo or alkyl)-5-aryl-2,4-thiazolidinedione and oxazolidinedione derivatives as PPAR agonists
INVENTOR(S): Sahoo, Souyma P.; Santini, Conrad; Boueres, Julia K.; Heck, James V.; Metzger, Edward; Lombardo, Victoria K.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078312	A1	20001228	WO 2000-US16586	20000616 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2376919	A1	20001228	CA 2000-2376919	20000616 <--
EP 1194146	A1	20020410	EP 2000-944694	20000616 <--
EP 1194146	B1	20060719		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
US 6399640	B1	20020604	US 2000-595802	20000616 <--

JP 2003502369	T	20030121	JP 2001-504375		20000616 <--
AU 773505	B2	20040527	AU 2000-58755		20000616
AT 333448	T	20060815	AT 2000-944694		20000616
ES 2265952	T3	20070301	ES 2000-944694		20000616
PRIORITY APPLN. INFO.:			US 1999-139953P	P	19990618
			WO 2000-US16586	W	20000616

OTHER SOURCE(S): MARPAT 134:71589

AB The title compds. (I) [wherein Ar1 = (hetero)arylene optionally substituted with 1-4 R1 groups; Ar2 = (hetero)aryl substituted with 1-5 Ra groups; X and Y = independently O, S, NRb, or CH2; Z = O or S; n = 0-3; R = (un)substituted alkyl, F, or Cl; Ra = halo, ORb, (hetero)aryl, or (un)substituted alkanoyl, alkyl, alkenyl, alkynyl, or heterocyclyl; Rb = H, (hetero)aryl, (hetero)arylalkyl, alkanoyl, cycloalkyl, or (un)substituted alkyl, alkenyl, or alkynyl] were prepared as peroxisome proliferator activated receptor (PPAR) agonists. For example, 4-(3-bromopropoxy)-3-propylphenyl Ph ether and Me 3-hydroxyphenylacetate were coupled. The acetate was α-brominated with N-bromosuccinimide and then treated with thiourea and NaOAc in MeOEt to give the 5-aryl-2,4-thiazolidinedione cycloaddn. product. Fluorination with N-fluorobenzenesulfonimide in the presence of KOBu-t in DMF, followed by addition of NaN(TMS)2, afforded the 5-aryl-5-fluoro-2,4-thiazolidinedione (II). I are useful in the treatment, control, or prevention of diabetes, hyperglycemia, hyperlipidemia (including hypercholesterolemia and hypertriglyceridemia), atherosclerosis, obesity, vascular restenosis, and other PPAR α and/or γ mediated diseases, disorders, and conditions (no data).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:362595 CAPLUS
DOCUMENT NUMBER: 133:13403
TITLE: Adipocyte containing ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases
INVENTOR(S): Briggs, Michael R.; Auwerx, Johan; De Vos, Piet; Staels, Bart; Croston, Glenn E.; Miller, Stephen G.
PATENT ASSIGNEE(S): Ligand Pharmaceuticals Inc., USA
SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 558,588, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6068976	A	20000530	US 1996-618100		19960319 <--
CA 2215387	A1	19960926	CA 1996-2215387		19960319 <--
PRIORITY APPLN. INFO.:			US 1995-408584	B2	19950320
			US 1995-418096	B2	19950405
			US 1995-510584	B2	19950802
			US 1995-558588	B2	19951030
			US 1995-7390P	P	19951121
			US 1995-7721P	P	19951130
			US 1995-8601P	P	19951214

AB This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a method for identifying and screening for agents useful for the treatment of diseases and pathol. conditions affected by the level of expression of an ob gene.

These agents interact directly or indirectly with the promoter or other control regions of the ob gene. A PPARγ agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body weight loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, diabetes, hypertension, cardiovascular diseases and infertility.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:235624 CAPLUS
DOCUMENT NUMBER: 133:870
TITLE: Androgens and liver function
AUTHOR(S): Bradlow, H. Leon; Zumoff, Barnett
CORPORATE SOURCE: Strang Cornell Cancer Research Laboratory, New York, NY, USA
SOURCE: Dehydroepiandrosterone (DHEA) (2000), 363-375. Editor(s): Kalimi, Mohammed; Regelson, William. Walter de Gruyter GmbH & Co. KG: Berlin, Germany.
CODEN: 68TYAR
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review, with 95 refs. The following topics were discussed: anti-obesity and anticancer effects of dehydroepiandrosterone (DHEA) and its metabolites; DHEA as a peroxisome proliferator; and normal regulatory actions of androgens in the liver.
REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:807315 CAPLUS
DOCUMENT NUMBER: 132:246176
TITLE: Peroxisome proliferators as adjuvants for the reverse-electron-transport therapy of obesity: an explanation for the large increase in metabolic rate of MEDICA 16-treated rats
AUTHOR(S): McCarty, M. F.
CORPORATE SOURCE: Nutrition 21/AMBI, San Diego, CA, 92109, USA
SOURCE: Medical Hypotheses (1999), 53(4), 272-276
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The efficacy of reverse-electron-transport therapy of obesity should be promoted by agents which up-regulate hepatocyte enzymes that are potentially rate-limiting for mitochondrial fatty acid oxidation and electron shuttles. Peroxisome proliferator drugs, including the fibrates used to treat hyperlipidemia, may be useful in this regard, as they induce malic enzyme, the mitochondrial glycerol-3-phosphate dehydrogenase, and carnitine palmitoyl transferase I in rodent hepatocytes. An agent of this class, MEDICA 16, has the addnl. property of potently inhibiting both citrate lyase and acetyl-CoA carboxylase. As a result, methyl-substituted dicarboxylic acids (MEDICA) 16 can be expected to disinhibit hepatic fatty acid oxidation while up-regulating electron shuttle mechanisms, and thus should stimulate reverse electron transport. This may explain the remarkable 40% increase in basal metabolic rate observed in normal rats ingesting MEDICA 16 - an effect not associated with any compensatory increase in food intake. Relative to controls, the MEDICA 16-treated rats achieved a 50% reduction in body fat and a modest increase in lean mass, such that weight

and growth were not changed. In other rodent strains, MEDICA 16 has prevented obesity diabetes and atherogenesis. However, whether MEDICA 16 and other peroxisome proliferator drugs will have clin. utility in reverse-electron-transport therapy may hinge on their ability to induce key enzymes in human hepatocytes; cell culture studies to evaluate this are required.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:789202 CAPLUS
DOCUMENT NUMBER: 132:117393
TITLE: Chronic and acute effects of thiazolidinediones BM13.1258 and BM15.2054 on rat skeletal muscle glucose metabolism
AUTHOR(S): Furnsinn, C.; Brunmair, B.; Meyer, M.; Neschen, S.; Furtmuller, R.; Roden, M.; Kuhnle, H. F.; Nowotny, P.; Schneider, B.; Waldhausl, W.
CORPORATE SOURCE: Division of Endocrinology & Metabolism, Department of Medicine III, Vienna, A-1090, Austria
SOURCE: British Journal of Pharmacology (1999), 128(6), 1141-1148
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 New thiazolidinediones BM13.1258 and BM15.2054 were studied with regard to their PPARγ-agonistic activities and to their acute and chronic effects on glucose metabolism in soleus muscle strips from lean and genetically obese rats. 2 Both BM13.1258 and BM15.2054 revealed to be potent PPARγ-activators in transient transfection assays in vitro. 3 In insulin-resistant obese rats, but not in lean rats, 10 days of oral treatment with either compound increased the stimulatory effect of insulin on muscle glycogen synthesis to a similar extent (insulin-induced increment in μmol glucose incorporated into glycogen g-1 h-1: control, +1.19±0.28; BM13.1258, +2.50±0.20; BM15.2054, +2.55±0.46; P<0.05 vs control each). 4 In parallel to insulin sensitization, mean glucose oxidation increased insulin independently in response to BM13.1258 (to 191 and 183% of control in the absence and presence of insulin, resp.; P<0.01 each), which was hardly seen in response to BM15.2054 (to 137 and 124% of control, resp.; ns). 5 Comparable effects on PPARγ activation and on amelioration of insulin resistance by BM13.1258 and BM15.2054 were therefore opposed by different effects on glucose oxidation 6 In contrast to chronic oral treatment, acute exposure of muscles to BM13.1258 or BM15.2054 in vitro elicited a distinct catabolic response of glucose metabolism in specimens from both lean and obese rats. 7 The results provide evidence that BM13.1258 and BM15.2054 can affect muscle glucose metabolism via more than one mechanism of action. 8 Further efforts are required to clarify, to what extent other mechanisms besides insulin sensitization via the activation of PPARγ are involved in the antidiabetic actions of thiazolidinediones.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:446177 CAPLUS
DOCUMENT NUMBER: 131:209060
TITLE: Rosiglitazone (BRL49653), a PPARγ-selective agonist, causes peroxisome proliferator-like liver effects in obese mice
AUTHOR(S): Edvardsson, Ulrika; Bergstrom, Monica; Alexandersson,

Maria; Bamberg, Krister; Ljung, Bengt; Dahllof, Bjorn
CORPORATE SOURCE: Cell Biology and Biochemistry, Astra Hassle AB, Moelndal, S-431 83, Swed.
SOURCE: Journal of Lipid Research (1999), 40(7), 1177-1184
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The PPAR (peroxisome proliferator activated receptor) transcription factors are ligand-activated nuclear receptors that regulate genes involved in lipid metabolism and homeostasis. PPARα is preferentially expressed in liver and PPARγ preferentially in adipose tissue. Activation of PPARα leads to peroxisome proliferation and increased β-oxidation of fatty acids in rodents. PPARγ-activation leads to adipocyte differentiation and improved insulin signaling of mature adipocytes. Both PPAR receptors are believed to be functional targets for treatment of hyperlipidemia in man. The authors have treated obese diabetic mice (ob/ob), which have highly elevated levels of plasma triglycerides, glucose and insulin, for 1 wk with WY14,643 (180 μmol/kg/day), a selective PPARα agonist, or rosiglitazone (BRL49653; 2.5 μmol/kg/day), a selective PPARγ agonist. The doses used produce a similar therapeutic effect in both treatment groups (lowering of triglycerides and glucose). High resolution two-dimensional gel electrophoresis of livers showed that WY14,643 and rosiglitazone both produced changes in expression pattern of many proteins involved in peroxisomal fatty acid β-oxidation However, similar expts. performed in lean mice showed significant up-regulation of these proteins only with WY14,643 treatment. Furthermore, the proteins up-regulated by the drugs in obese mice had a higher basal expression in obese controls compared to the lean littermates. Liver PPARγ mRNA levels were determined and the authors observed that PPARγ2 mRNA levels were elevated in obese mice compared to lean littermates. As PPARα and PPARγ recognize similar DNA response elements, it is likely that the effects of rosiglitazone on PPARα responsive genes in livers of the ob/ob mice are mediated by PPARγ2.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:736960 CAPLUS
DOCUMENT NUMBER: 130:93928
TITLE: Peroxisome proliferator-activated receptor α-isoform deficiency leads to progressive dyslipidemia with sexually dimorphic obesity and steatosis
AUTHOR(S): Costet, Philippe; Legendre, Christiane; More, Jean; Edgar, Alan; Galtier, Pierre; Pineau, Thierry
CORPORATE SOURCE: Laboratoire de Pharmacologie et Toxicologie, INRA, Toulouse, 31931, Fr.
SOURCE: Journal of Biological Chemistry (1998), 273(45), 29577-29585
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The α-isoform of the peroxisome proliferator-activated receptor (PPARα) is a nuclear transcription factor activated by structurally diverse chems. referred to as peroxisome proliferators . Activators can be endogenous mols. (fatty acids/steroids) or

xenobiotics (fibrate lipid-lowering drugs). Upon pharmacol. activation, PPARα modulates target genes encoding lipid metabolism enzymes, lipid transporters, or apolipoproteins, suggesting a role in lipid homeostasis. Transgenic mice deficient in PPARα were shown to lack hepatic peroxisomal proliferation and have an impaired expression and induction of several hepatic target genes. Young adult males show hypercholesterolemia but normal triglycerides. Using a long term exptl. set up, the authors identified these mice as a model of monogenic, spontaneous, late onset obesity with stable caloric intake and a marked sexual dimorphism. Serum triglycerides, elevated in aged animals, are higher in females that develop a more pronounced obesity than males. The latter show a marked and original centrilobular-restricted steatosis and a delayed occurrence of obesity. Fat cells from their liver express substantial levels of PPARγ2 transcripts when compared with lean cells. These studies demonstrate, in rodents, the involvement of PPARα nuclear receptor in lipid homeostasis, with a sexually dimorphic control of circulating lipids, fat storage, and obesity . Characterization of this pathol. link may help to delineate new mol. targets for therapeutic intervention and could lead to new insights into the etiol. and heritability of mammalian obesity.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:835847 CAPLUS
DOCUMENT NUMBER: 123:281583
ORIGINAL REFERENCE NO.: 123:50363a,50366a
TITLE: Toward the treatment of obesity. Role of PPARγ in adipogenesis
AUTHOR(S): Motojima, Kiyoto
CORPORATE SOURCE: Sch. Pharm. Sci., Toho Univ., Funabashi, 274, Japan
SOURCE: Tanpakushitsu Kakusan Koso (1995), 40(13), 1936-41
CODEN: TAKKAJ; ISSN: 0039-9450
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 32 refs., on the function of peroxisomes and carcinogenicity of peroxisome proliferators, cDNA cloning of peroxisome proliferator-activated receptor (PPAR), structure and mol. diversity of PPAR subtypes, roles of PPAR and peroxisome proliferators in adipocyte differentiation, and function of PPARγ as a transcription factor. Inhibitors or activators of PPARγ may be able to control adipogenesis and can be useful drugs for treatment or prevention of obesity.

=> s antioxidants
118752 ANTIOXIDANTS
1 ANTIOXIDANTSES
L10 118753 ANTIOXIDANTS
(ANTIOXIDANTS OR ANTIOXIDANTSES)

=> d his

(FILE 'HOME' ENTERED AT 23:21:40 ON 27 JUN 2008)

FILE 'REGISTRY' ENTERED AT 23:21:50 ON 27 JUN 2008
E ROSIGLITAZONE
L1 9 S E3
E "COENZYME Q10"

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     FILE 'CAPLUS' ENTERED AT 23:23:04 ON 27 JUN 2008
L2            92 S L1 AND ANTIOXIDANT
L3             4 S L2 AND "COENZYME Q10"
L4            22 S L2 AND 1960<=PY<=2003
L5            22 DUP REM L4 (0 DUPLICATES REMOVED)
                 E PPAR AGONISTS+ALL/CT
L6          2471 S (PPAR AGONISTS OR "PEROXISOME PROLIFERATORS")
L7          2471 S ("PPAR AGONISTS" OR "PEROXISOME PROLIFERATORS")
L8           266 S L7 AND OBESITY
L9            24 S L8 AND 1960<=PY<=2003
L10       118753 S ANTIOXIDANTS

=> s l7 and l10
L11         117 L7 AND L10

=> S L11 AND 1960<=PY<=2003
      21227234 1960<=PY<=2003
L12          30 L11 AND 1960<=PY<=2003

=> d L12 1-30 ibib ab

L12  ANSWER 1 OF 30  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:620087  CAPLUS
DOCUMENT NUMBER:          147:16717
TITLE:                    Progenitor endothelial cell capturing with a
                          drug-eluting implantable medical device
INVENTOR(S):              Cottone, Robert John, Jr.; Rowland, Stephen M.;
                          Parker, Sherry
PATENT ASSIGNEE(S):       Orbusneich Medical, Inc., USA
SOURCE:                   U.S. Pat. Appl. Publ., 47pp., Cont.-in-part of U.S.
                          Ser. No. 76,731.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   13
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     US 20070129789       A1    20070607    US 2006-561730         20061120
     US 20020049495       A1    20020425    US 2001-808867         20010315 <--
     US 7037332           B2    20060502
     US 20030229393       A1    20031211    US 2003-360567         20030206 <--
     WO 2003099169        A1    20031204    WO 2003-US15811        20030520 <--
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
              FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
              BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003241515        A1    20031212    AU 2003-241515         20030520 <--
     US 20040039441       A1    20040226    US 2003-442669         20030520
     CN 1655738           A     20050817    CN 2003-811531         20030520
     JP 2005525911        T     20050902    JP 2004-506697         20030520
     US 20050271701       A1    20051208    US 2005-76731          20050310
     US 20070134290       A1    20070614    US 2006-494801         20060726
     US 20070156232       A1    20070705    US 2006-562931         20061122
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PRIORITY APPLN. INFO.:	US 2000-189674P	P 20000315
	US 2000-201789P	P 20000504
	US 2001-808867	A2 20010315
	US 2002-354680P	P 20020206
	US 2002-382095P	P 20020520
	US 2003-360567	A2 20030206
	US 2003-442669	B2 20030520
	US 2004-551978P	P 20040310
	US 2005-76731	A2 20050310
	US 2006-822451P	P 20060815
	WO 2003-US15811	W 20030520
	US 2004-832106	A1 20040426

AB A medical device for implantation into vessels or luminal structures within the body is provided, which stimulates pos. blood vessel remodeling. The medical device, such as a stent and a synthetic graft, is coated with a pharmaceutical composition consisting of a controlled-release matrix and one or more pharmaceutical substances for direct delivery of drugs to surrounding tissues. The coating on the medical device further comprises a ligand such as a peptide, an antibody or a small mol. for capturing progenitor endothelial cells in the blood contacting surface of the device for restoring an endothelium at the site of injury. In particular, the drug-coated stents are for use, for example, in balloon angioplasty procedures for preventing or inhibiting restenosis.

L12 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2007:151052 CAPLUS
DOCUMENT NUMBER:	146:244343
TITLE:	Peptides and peptide mimetics to treat pathologies characterized by an inflammatory response
INVENTOR(S):	Fogelman, Alan M.; Navab, Mohamad
PATENT ASSIGNEE(S):	The Regents of the University of California, USA
SOURCE:	U.S. Pat. Appl. Publ., 313pp., Cont.-in-part of U.S. Ser. No. 423,830. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	9
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20070032430	A1	20070208	US 2006-407390	20060418	
US 6664230	B1	20031216	US 2000-645454	20000824	<--
US 20030045460	A1	20030306	US 2001-896841	20010629	<--
US 6933279	B2	20050823			
CN 1375299	A	20021023	CN 2001-103876	20010823	<--
CN 1739787	A	20060301	CN 2005-10103876	20010823	
CN 1911439	A	20070214	CN 2006-10100670	20010823	
CN 1931358	A	20070321	CN 2006-10100667	20010823	
CN 1931359	A	20070321	CN 2006-10100669	20010823	
CN 1943781	A	20070411	CN 2006-10100668	20010823	
EP 1864675	A1	20071212	EP 2007-7775	20010823	
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR					
US 20030171277	A1	20030911	US 2002-187215	20020628	<--
US 7144862	B2	20061205			
US 20030229015	A1	20031211	US 2002-273386	20021016	<--
US 7166578	B2	20070123			
US 20040266671	A1	20041230	US 2003-423830	20030425	
US 7199102	B2	20070403			
JP 2006056899	A	20060302	JP 2005-304531	20051019	

JP 2006312650	A	20061116	JP 2006-220831		20060814
JP 2007277250	A	20071025	JP 2007-118451		20070427
US 20080095821	A1	20080424	US 2007-830497		20070730
AU 2007237157	A1	20071213	AU 2007-237157		20071126
PRIORITY APPLN. INFO.:			US 2000-645454	A2	20000824
			US 2001-896841	A2	20010629
			US 2002-187215	A2	20020628
			US 2002-273386	A2	20021016
			US 2003-423830	A2	20030425
			US 2005-676431P	P	20050429
			US 2005-697495P	P	20050707
			CN 2001-103876	A3	20010823
			CN 2001-817280	A3	20010823
			CN 2005-10103876	A3	20010823
			EP 2001-966198	A3	20010823
			JP 2002-520844	A3	20010823
			WO 2001-US26497	A2	20010823
			JP 2005-304531	A3	20051019
			AU 2006-200035	A3	20060106
			US 2006-407390	A1	20060418
			JP 2006-220831	A3	20060814

OTHER SOURCE(S): MARPAT 146:244343

AB The invention provides novel active agents (e.g. peptides, small organic mols., amino acid pairs, etc.) that ameliorate one or more symptoms of atherosclerosis and/or other pathologies characterized by an inflammatory response. In certain embodiments, the peptides resemble a G* amphipathic helix of apolipoprotein J. The agents are highly stable and readily administered via an oral route. Peptide preparation is included.

L12 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1178595 CAPLUS
DOCUMENT NUMBER: 146:740
TITLE: Peptides and peptide mimetics to treat pathologies characterized by an inflammatory response
INVENTOR(S): Fogelman, Alan M.; Navab, Mohamad
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 143pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006118805	A2	20061109	WO 2006-US14839	20060418
WO 2006118805	A9	20070118		
WO 2006118805	A3	20070607		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
CN 1375299	A	20021023	CN 2001-103876	20010823 <--

AU 2006242651	A1	20061109	AU 2006-242651		20060418
CA 2607483	A1	20061109	CA 2006-2607483		20060418
EP 1890715	A2	20080227	EP 2006-750791		20060418
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR					
MX 200713430	A	20080319	MX 2007-13430		20071026
IN 2007KN04199	A	20080215	IN 2007-KN4199		20071101
NO 2007006022	A	20080128	NO 2007-6022		20071122
AU 2007237157	A1	20071213	AU 2007-237157		20071126
KR 2008007491	A	20080121	KR 2007-727948		20071129
PRIORITY APPLN. INFO.:			US 2005-676431P	P	20050429
			US 2005-697495P	P	20050707
			AU 2006-200035	A3	20060106
			WO 2006-US14839	W	20060418

AB This invention provides novel active agents (e.g. peptides, small organic mols., amino acid pairs, etc.) peptides that ameliorate one or more symptoms of atherosclerosis and/or other pathologies characterized by an inflammatory response. In certain embodiment, the peptides resemble a G* amphipathic helix of apolipoprotein J. The agents are highly stable and readily administered via an oral route. Synthetic procedures are described.

L12 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2006:1124321 CAPLUS
DOCUMENT NUMBER:	145:460611
TITLE:	Delivery of highly lipophilic agents via medical devices
INVENTOR(S):	Cromack, Keith R.; Toner, John L.; Burke, Sandra E.; Krasula, Richard W.; Schwartz, Lewis B.
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 49pp., Cont.-in-part of U.S. Ser. No. 977,288. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	17
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20060240070	A1	20061026	US 2006-386587	20060322	
US 6015815	A	20000118	US 1998-159945	19980924	<--
US 6329386	B1	20011211	US 1999-433001	19991102	<--
US 20020123505	A1	20020905	US 2001-950307	20010910	<--
US 6890546	B2	20050510			
US 20030129215	A1	20030710	US 2002-235572	20020906	<--
US 20040180039	A1	20040916	US 2004-796243	20040309	
US 20050175660	A1	20050811	US 2004-977288	20041029	
EP 1877004	A2	20080116	EP 2006-739478	20060322	
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
WO 2007046935	A2	20070426	WO 2006-US31879	20060815	
WO 2007046935	A3	20070705			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW					

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EP 1933785 A2 20080625 EP 2006-813474 20060815

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

WO 2007047416 A2 20070426 WO 2006-US40027 20061012

WO 2007047416 A3 20071108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

WO 2007047473 A2 20070426 WO 2006-US40155 20061012

WO 2007047473 A3 20070809

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 1933759 A2 20080625 EP 2006-816907 20061012

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

EP 1933760 A2 20080625 EP 2006-825887 20061012

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

WO 2007111885 A2 20071004 WO 2007-US6916 20070319

WO 2007111885 A3 20071206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 1998-159945 A3 19980924
US 1999-433001 A2 19991102
US 2001-950307 A2 20010910
US 2002-235572 A2 20020906
US 2003-453555P P 20030310

US 2004-769243	A2	20040130
US 2004-796243	A2	20040309
US 2004-977288	A2	20041029
US 2005-664328P	P	20050323
US 2005-726878P	P	20051014
US 2005-727080P	P	20051014
US 2005-727196P	P	20051014
US 2005-732577P	P	20051017
US 1997-60105P	P	19970926
US 2005-664488P	P	20050323
US 2005-715082P	P	20050908
US 2006-386587	A	20060322
WO 2006-US10700	W	20060322
WO 2006-US31879	W	20060815
WO 2006-US40027	W	20061012
WO 2006-US40155	W	20061012

AB An apparatus and system for delivering a lipophilic agent associated with a medical device including: a medical device, a first lipophilic agent capable of penetrating a body lumen, wherein the transfer coeffs. of the first lipophilic agent is by an amount that is statistically significant of at least approx. 5,000, wherein the first lipophilic agent is associated with the medical device, wherein the first lipophilic agent/medical device is placed adjacent to said body lumen, and wherein a therapeutically effective amount of the first lipophilic agent is delivered to a desired area within a subject. Furthermore, the invention relates to a method for improving patency in a subject involving placement of a medical device in a body lumen for treating and/or preventing adjacent diseases or maintaining patency of the body lumen.

L12 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1004266 CAPLUS
DOCUMENT NUMBER: 143:299112
TITLE: Apolipoprotein or serum amyloid A-derived helical synthetic peptides that stimulate cellular cholesterol efflux for therapeutic use
INVENTOR(S): Bielicki, John K.; Natarajan, Pradeep
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 74 pp., Cont.-in-part of U.S. Ser. No. 142,238.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050202532	A1	20050915	US 2004-14187	20041215
US 20030087819	A1	20030508	US 2002-142238	20020508 <--
US 7217785	B2	20070515		
PRIORITY APPLN. INFO.:			US 2002-142238	A2 20020508
			US 2003-529933P	P 20031215
			US 2001-289944P	P 20010509

AB The present invention provides peptides comprising at least one amphipathic alpha helix and having a cholesterol mediating activity and an ATP-binding cassette transporter A (ABCA) stabilization activity. The peptide may be a fragment of an apolipoprotein or serum amyloid A. The peptides have antioxidant and anti-inflammatory activity and may be used with other therapeutic agents for treating cardiovascular disease.

L12 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2850 CAPLUS
DOCUMENT NUMBER: 140:77013
TITLE: Preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia
INVENTOR(S): Jaehne, Gerhard; Frick, Wendelin; Flohr, Stefanie; Lindenschmidt, Andreas; Glombik, Heiner; Kramer, Werner; Heuer, Hubert; Schaefer, Hans-Ludwig
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000804	A1	20031231	WO 2003-EP5815	20030604 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10227506	A1	20040108	DE 2002-10227506	20020619
CA 2490109	A1	20031231	CA 2003-2490109	20030604 <--
AU 2003242616	A1	20040106	AU 2003-242616	20030604
EP 1517892	A1	20050330	EP 2003-760591	20030604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011940	A	20050405	BR 2003-11940	20030604
CN 1662493	A	20050831	CN 2003-814087	20030604
NZ 537304	A	20051028	NZ 2003-537304	20030604
JP 2005533072	T	20051104	JP 2004-514660	20030604
RU 2315754	C2	20080127	RU 2005-101091	20030604
US 20040082561	A1	20040429	US 2003-463807	20030618
US 7176194	B2	20070213		
MX 2004PA12236	A	20050225	MX 2004-PA12236	20041207
IN 2004CN02826	A	20060210	IN 2004-CN2826	20041214
NO 2005000073	A	20050106	NO 2005-73	20050106
ZA 2004009381	A	20060531	ZA 2004-9831	20060403
US 20060270613	A1	20061130	US 2006-501758	20060810
US 20070037787	A1	20070215	US 2006-544746	20061010
US 20070043017	A1	20070222	US 2006-544718	20061010
US 7390790	B2	20080624		

PRIORITY APPLN. INFO.:

DE 2002-10227506	A	20020619
US 2002-411984P	P	20020919
WO 2003-EP5815	W	20030604
US 2003-463807	A1	20030618

OTHER SOURCE(S): MARPAT 140:77013

AB Title compds. I [R1, R2, R3, R4, R5, R6 = (un)substituted alkylene-(LAG)n; n = 1-5; LAG = sugar; amino sugar; amino acid, etc.] and their pharmaceutically acceptable salts were prepared For example, N-alkylation of 1,4-diazabicyclo[2.2.2]octane with benzyl bromide II, e.g., prepared from 1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-2-azetidinone and 1,2-bisbromomethylbenzene, afforded

diphenylazetidinone III. In rat liver chloresterol absorption assays, 26-examples of compds. I exhibited EC50 values ranging from 0.03-<1.0 (mg/mouse), e.g., the EC50 value of diphenylazetidinone III was 0.3. Compds. I are claimed useful for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2849 CAPLUS

DOCUMENT NUMBER: 140:77012

TITLE: Preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia

INVENTOR(S): Jaehne, Gerhard; Frick, Wendelin; Flohr, Stefanie; Lindenschmidt, Andreas; Glombik, Heiner; Kramer, Werner; Heuer, Hubert; Schaefer, Hans-ludwig

PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000803	A1	20031231	WO 2003-EP5814	20030604 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10227507	A1	20040108	DE 2002-10227507	20020619
CA 2490108	A1	20031231	CA 2003-2490108	20030604 <--
AU 2003238209	A1	20040106	AU 2003-238209	20030604
EP 1517890	A1	20050330	EP 2003-735534	20030604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011984	A	20050426	BR 2003-11984	20030604
CN 1662494	A	20050831	CN 2003-814093	20030604
JP 2005533071	T	20051104	JP 2004-514659	20030604
NZ 537303	A	20060630	NZ 2003-537303	20030604
RU 2315753	C2	20080127	RU 2005-101088	20030604
US 20040077623	A1	20040422	US 2003-463789	20030618
MX 2004PA12308	A	20050225	MX 2004-PA12308	20041208
IN 2004CN02844	A	20060210	IN 2004-CN2844	20041215
NO 2005000088	A	20050106	NO 2005-88	20050106
ZA 2004009379	A	20060531	ZA 2004-9379	20060403

PRIORITY APPLN. INFO.:

DE 2002-10227507	A	20020619
US 2002-411981P	P	20020919
WO 2003-EP5814	W	20030604

OTHER SOURCE(S): MARPAT 140:77012

AB Title compds. I [R1, R2, R3, R4, R5, R6 = (un)substituted alkylene-(LAG)n; n = 1-5; LAG = sugar; amino sugar; amino acid, etc.] and their pharmaceutically acceptable salts were prepared For example, condensation

of benzonitrile II e.g., prepared from 3-[5-(4-fluorophenyl)-5-hydroxypentanoyl]-4-phenyloxazolidin-2-one in 4-steps, and hydroxylamine hydrochloride afforded N-hydroxybenzenecarboximidamide III. In rat liver cholesterol absorption assays, 14-examples of compds. I exhibited EC50 values ranging from 0.03-<1.0 (mg/mouse), e.g., the EC50 value of N-hydroxybenzenecarboximidamide III was 0.1. Compds. I are claimed useful for the treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:991491 CAPLUS

DOCUMENT NUMBER: 140:27832

TITLE: Preparation of triazolyl 11β-hydroxysteroid dehydrogenase-1 inhibitors for the treatment of diabetes, obesity and dyslipidemia

INVENTOR(S): Olson, Steven H.; Balkovec, James M.; Zhu, Yuping

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003104208	A1	20031218	WO 2003-US17890	20030606 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2488592	A1	20031218	CA 2003-2488592	20030606 <--
AU 2003251410	A1	20031222	AU 2003-251410	20030606 <--
EP 1532122	A1	20050525	EP 2003-757385	20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1659151	A	20050824	CN 2003-813392	20030606
CN 1990474	A	20070704	CN 2007-10003770	20030606
US 20040048912	A1	20040311	US 2003-457682	20030609
US 6730690	B2	20040504		
US 20040106664	A1	20040603	US 2003-697547	20031030
US 7179802	B2	20070220		
ZA 2004008772	A	20051118	ZA 2004-8772	20041029

PRIORITY APPLN. INFO.:

US 2002-387385P	P	20020610
CN 2003-813392	A3	20030606
WO 2003-US17890	W	20030606
US 2003-457682	A3	20030609

OTHER SOURCE(S): MARPAT 140:27832

AB Title compds. I [A = halo, alkyl, Ph, etc.; B = H, halo, alkyl, S-alkyl, etc. or A, B = taken together are (un)substituted alkylene; R1 = H, OH, halo, alkyl, alkoxy, aryl, etc.; R2 = alkyl, alkoxy, Ph, etc.; R3 = alkyl, alkenyl, thioalkoxy, aryl, heterocyclyl, etc. or R2-3 = taken together fused 5-6-membered alkyl/aryl ring] are prepared For instance,

2,2-diphenylbutanoic acid is converted to the corresponding hydrazide (DMF, Et3N, TFFH, H2NNH2, 0°, 30 min). 8-Methoxy-2,3,4,5,6,7-hexahydroazocine is then reacted with the intermediate (DMF, 120°, overnight) to give II. Example compds. exhibit IC50 < 500 nM for 11β-hydroxysteroid dehydrogenase-1 (11β-HSD1). I are useful for the treatment of diabetes, such as noninsulin-dependent diabetes (NIDDM), hyperglycemia, obesity, insulin resistance, dylsipidemia, hyperlipidemia, hypertension, Syndrome X and other symptoms associated with NIDDM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:829064 CAPLUS
DOCUMENT NUMBER: 140:175071
TITLE: Protective effects of green tea polyphenols on human HepG2 cells against oxidative damage of fenofibrate
AUTHOR(S): Jiao, Hong-li; Ye, Ping; Zhao, Bao-lu
CORPORATE SOURCE: Institute of Biophysics, Research Centers of Brain and Cognitive Science, Laboratory of Visual Information Processing, The Chinese Academy of Sciences, Beijing, Peop. Rep. China
SOURCE: Free Radical Biology & Medicine (2003), 35(9), 1121-1128
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this work was to investigate the protective effects of green tea polyphenols on the cytotoxic effects of hypolipidemic agent fenofibrate (FF), a peroxisome proliferator (PP), in human HepG2 cells. The results showed that high concns. of FF induced human HepG2 cell death through a mechanism involving an increase of reactive oxygen species (ROS) and intracellular reduced glutathione (GSH) depletion. These effects were partially prevented by antioxidant green tea polyphenols. The elevated expression of PP-activated receptors α (PPARα) in HepG2 cells induced by FF was also decreased by treatment with green tea polyphenols. In conclusion, this result demonstrates that oxidative stress and PPARα are involved in FF cytotoxicity and green tea polyphenols have a protective effect against FF-induced cellular injury. It may be beneficial for the hyperlipidemic patients who were administered the hypolipidemic drug fenofibrate to drink tea or use green tea polyphenols synchronously during their treatment.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:354632 CAPLUS
DOCUMENT NUMBER: 139:111244
TITLE: Does the release of arachidonic acid from cells play a role in cancer chemoprevention?
AUTHOR(S): Levine, Lawrence
CORPORATE SOURCE: Department of Biochemistry, Brandeis University, Waltham, MA, 02454, USA
SOURCE: FASEB Journal (2003), 17(8), 800-802
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB COX-2 is overexpressed in cancer cells and has become a major target for cancer preventive drugs. NSAIDs, retinoids, antioxidants, and

PPAR agonists, reported to be chemopreventive, suppress COX-2 synthesis. NSAIDs also have been shown to be chemopreventive independent of COX-2 activity. Common to all of these compds. is their ability to release arachidonic acid (AA) from rat liver cells in culture. Most of these compds. inhibit induced PGI2 production Vitamin D3 and tamoxifen, however, not only stimulate the release of AA from cells: they amplify rather than inhibits induced COX activity. In view of the many activities attributable to AA, I propose that its release and accumulation could initiate mol. reactions that lead to apoptosis and eventually to suppression of cancer. Some drugs shown to release AA from cells and affect PGI2 production-e.g., thiazolidinediones and statins are widely used for conditions unrelated to cancer. In vivo studies could reveal whether they can also function as cancer preventive agents.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:637640 CAPLUS
DOCUMENT NUMBER: 137:185320
TITLE: PPAR agonists, e.g., 3-[4-[2-[3-(2,4-dimethoxyphenyl)-1-heptylureido]ethyl]phenyl]-2-ethoxypropionic acid and analogs, useful particularly as PPARα agonists, and their pharmaceutical compositions and therapeutic use as hypolipemics, antidiabetics, etc.
INVENTOR(S): Hayward, Cheryl Myers; Perry, David Austen
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064549	A1	20020822	WO 2002-IB45	20020107 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2438551	A1	20020822	CA 2002-2438551	20020107 <--
AU 2002216330	A1	20020828	AU 2002-216330	20020107 <--
EP 1360172	A1	20031112	EP 2002-740089	20020107 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007285	A	20040210	BR 2002-7285	20020107
JP 2004529097	T	20040924	JP 2002-564482	20020107
US 20020165282	A1	20021107	US 2002-76740	20020214 <--
US 6699904	B2	20040302		
MX 2003PA07284	A	20031204	MX 2003-PA7284	20030814 <--

PRIORITY APPLN. INFO.:				
			US 2001-269058P	P 20010215
			WO 2002-IB45	W 20020107

OTHER SOURCE(S): MARPAT 137:185320

AB Title compds. I and their prodrugs and/or pharmaceutically acceptable salts are claimed [wherein: E = CO, SO2; B = CH2, NH; Z = CO2H, CHO,

CH2OH, alkoxycarbonyl, cyano, CONHOH, tetrazolyl, tetrazolylaminocarbonyl, 4,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl, 3-oxo-isoxazolidin-4-ylaminocarbonyl, CONHSO2R4; R1 = H, alkyl, cycloalkyl; R2 = H, cycloalkyl, (un)substituted and/or (un)saturated (hetero)aliphatic chain; R3 = (un)substituted alk(en/yn)yl; R4 = alkyl, amino or its (di)((poly)fluoro)alkyl derivs.; R5, R6 = H, alkyl, cycloalkyl, or cycloalkylalkyl; or R5R6 = atoms to form 3- to 6-membered fully saturated carbocyclic ring; A = H, (di)(alkyl)amino, alkanoylamino, alkoxy, or (un)substituted (un)saturated (bi)(hetero)cyclic ring; W = bond, NH, N-alkyl, alkylamino (sic), or alkylene; or W = CR7R8 where R7R8 = atoms to form 3- to 6-membered fully saturated carbocyclic ring]. The compds. are disclosed as PPAR (peroxisome proliferator-activated receptor) agonists, and particularly as PPARα activators (no data). Also disclosed are pharmaceutical compns. containing I, and the use of I to elevate certain plasma lipid levels, including high d. lipoprotein-cholesterol, and to lower certain other plasma lipid levels, such as LDL-cholesterol and triglycerides, and accordingly to treat diseases which are exacerbated by low levels of HDL cholesterol and/or high levels of LDL-cholesterol and triglycerides, such as atherosclerosis and cardiovascular diseases, in mammals, including humans. Further claimed uses include treatment of obesity, diabetes and related conditions, atherosclerosis, hypertension, inflammation, and thrombosis. The compds. may also be administered in combination with a variety of other enzyme inhibitors. A total of 77 synthetic examples cover production of various I and their intermediates. The (R)- and (S)-enantiomers of approx. 15 compds. are specifically claimed. For instance, [4-(2-heptylaminoethyl)phenyl]methanol (preparation in 3 steps given) underwent a sequence of: (1) N-protection with BOC, (2) O-oxidation with MnO2 to an aldehyde, (3) Wittig type reaction of the latter with Ph2P(:O)CH(OEt)CO2Et, (4) reduction of the resultant acrylate ester to a propionate ester, (5) removal of BOC, (6) carbamoylation with 2,4-dimethoxyphenyl isocyanate, and (7) alkaline hydrolysis of the Me ester, to give title compound II.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:575765 CAPLUS

DOCUMENT NUMBER: 137:140435

TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of diabetes and lipid disorders, and their preparation, pharmaceutical compositions, and use

INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20020103242	A1	20020801	US 2001-21667	20011029 <--
US 6713508	B2	20040330		
CA 2427610	A1	20020808	CA 2001-2427610	20011026 <--
WO 2002060434	A2	20020808	WO 2001-US49501	20011026 <--
WO 2002060434	A3	20030619		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002248221	A1	20020812	AU 2002-248221	20011026 <--
AU 2002248221	B2	20060817		
EP 1347755	A2	20031001	EP 2001-997102	20011026 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517938	T	20040617	JP 2002-560626	20011026
PRIORITY APPLN. INFO.:			US 2000-244698P	P 20001031
			WO 2001-US49501	W 20011026

OTHER SOURCE(S): MARPAT 137:140435

AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms (un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their preparation is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alkaline hydrolysis (100%), to give title compound II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a number of specific drugs, is claimed.

L12 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2001:676560 CAPLUS
DOCUMENT NUMBER:	135:215737
TITLE:	Perilla oil as PPAR stabilizer for treating skin and hair conditions
INVENTOR(S):	Menon, Gopinathan K.
PATENT ASSIGNEE(S):	Avon Products, Inc., USA
SOURCE:	PCT Int. Appl., 19 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	5
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001066067		A1	20010913	WO 2001-US7007	20010302 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2397183		A1	20010913	CA 2001-2397183	20010302 <--
EP 1265583		A1	20021218	EP 2001-914687	20010302 <--
EP 1265583		B1	20080514		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009074		A	20030603	BR 2001-9074	20010302 <--
MX 2002PA08725		A	20030414	MX 2002-PA8725	20020906 <--
PRIORITY APPLN. INFO.:				US 2000-521442	A 20000307
				WO 2001-US7007	W 20010302

AB The present invention is a method of treating skin or hair conditions, such as acne, blemishes, breakouts, cellulite, oily skin, oily hair, oily scalp, or any combination thereof, that comprises topically applying an effective amount of perilla oil to the affected area of the skin or hair. The topical application of perilla oil inhibits PPAR upregulation in skin cells, particularly PPARα upregulation. For example, human skin cells were used to determine the effect upon PPAR upregulation by known PPAR agonists and the compound of the present invention as measured by relative PPRE (Peroxisome Proliferator Response Element) activity. Preconfluent keratinocytes were transiently transfected with a PPRE-luciferase reporter construct together with a β-galactosidase. Four similar groups of cells were treated the following day for 24 h. The first group contained a vehicle having 0.05% DMSO, the second group was treated with G3, a PPARα agonist, the third group was treated with A4, perilla seed oil diluted 1:100 with DMSO, and the fourth group was treated with G3 and A4. The addition of a PPAR agonist (G3) nearly doubled the PPRE activity as compared to the vehicle. However, the addition of perilla seed oil (A4) completely prevented the upregulation of PPAR in the presence of G3.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:617987 CAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2400021	A1	20010823	CA 2001-2400021		20010214 <--
AU 2001038214	A5	20010827	AU 2001-38214		20010214 <--
AU 784722	B2	20060601			
EP 1259494	A1	20021127	EP 2001-910624		20010214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003523336	T	20030805	JP 2001-560192		20010214 <--
PRIORITY APPLN. INFO.:			US 2000-183593P	P	20000218
			WO 2001-US4636	W	20010214

OTHER SOURCE(S): MARPAT 135:180757

AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me α-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by saponification, afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) α and/or γ and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPARα and/or γ mediated diseases, disorders, and conditions (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2001:609685 CAPLUS
DOCUMENT NUMBER:	136:48266
TITLE:	Mechanism of clofibrate hepatotoxicity: mitochondrial damage and oxidative stress in hepatocytes
AUTHOR(S):	Qu, B.; Li, Q.-T.; Wong, K. P.; Tan, T. M. C.; Halliwell, B.
CORPORATE SOURCE:	Department of Biochemistry, National University of Singapore, Faculty of Medicine, Singapore, Singapore
SOURCE:	Free Radical Biology & Medicine (2001), 31(5), 659-669 CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER:	Elsevier Science Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Peroxisome proliferators have been found to induce hepatocarcinogenesis in rodents, and may cause mitochondrial damage. Consistent with this, clofibrate increased hepatic mitochondrial oxidative DNA and protein damage in mice. The present investigation aimed to study the mechanism by which this might occur by examining the effect of clofibrate

on freshly isolated mouse liver mitochondria and a cultured hepatocyte cell line, AML-12. Mitochondrial membrane potential ($\Delta\Psi m$) was determined by using the fluorescent dye 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethyl-benzimidazolylcarbocyanine iodide (JC-1) and tetramethylrhodamine Me ester (TMRM). Application of clofibrate at concns. greater than 0.3 mM rapidly collapsed the $\Delta\Psi m$ both in liver cells and in isolated mitochondria. The loss of $\Delta\Psi m$ occurred prior to cell death and appeared to involve the mitochondrial permeability transition (MPT), as revealed by calcein fluorescence studies and the protective effect of cyclosporin A (CsA) on the decrease in $\Delta\Psi m$. Levels of reactive oxygen species (ROS) were measured with the fluorescent probes 5-(and-6)-carboxy-2',7'-dichlorofluorescein diacetate (DCFDA) and dihydrorhodamine 123 (DHR123). Treatment of the hepatocytes with clofibrate caused a significant increase in intracellular and mitochondrial ROS. Antioxidants such as vitamin C, deferoxamine, and catalase were able to protect the cells against the clofibrate-induced loss of viability, as was CsA, but to a lesser extent. These results suggest that one action of clofibrate might be to impair mitochondrial function, so stimulating formation of ROS, which eventually contribute to cell death.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:207545 CAPLUS
DOCUMENT NUMBER: 135:70813
TITLE: Growth reduction in glioma cells after treatment with tetradecylthioacetic acid: changes in fatty acid metabolism and oxidative status
AUTHOR(S): Tronstad, K. J.; Berge, K.; Dyroy, E.; Madsen, L.; Berge, R. K.
CORPORATE SOURCE: Department of Clinical Biochemistry, Haukeland Hospital, University of Bergen, Bergen, N-5021, Norway
SOURCE: Biochemical Pharmacology (2001), 61(6), 639-649
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During aerobic metabolism, a small amount of partially reduced oxygen is produced, yielding reactive oxygen species (ROS). Peroxisomes and mitochondria are major contributors to cellular ROS production, which is normally balanced by consumption by antioxidants. The fatty acid analog tetradecylthioacetic acid (TTA) promotes mitochondrial and peroxisomal proliferation, and may induce oxidative stress and change the growth potential of cancer cells. In the present study, we found that TTA reduced [3H]thymidine incorporation in the glioma cell lines BT4Cn (rat), D54Mg (human), and GaMg (human) in a dose- and time-dependent manner. The 50% inhibitory TTA doses were approx. 125 μM for BT4Cn and D54Mg cells and 40 μM for GaMg cells after 4 days. α-Tochopherol counteracted this inhibition in GaMg cells. TTA enhanced the oxidation of [1-14C]palmitic acid, which could be explained by stimulation of enzymes involved in peroxisomal (fatty acyl-CoA oxidase) and/or mitochondrial (carnitine palmitoyltransferase) fatty acid oxidation The glutathione content and the activities of glutathione peroxidase, glutathione reductase, and glutathione S-transferase were differentially affected. Increased malondialdehyde (MDA) production was seen in TTA-treated GaMg and D54Mg cells, but not in BT4Cn cells, in vitro. In BT4Cn tumor tissue from TTA-treated rats, MDA was increased while the α-tocopherol content tended to decrease. TTA increased the level of cytosolic cytochrome c in BT4Cn cells, which suggests induction of apoptotic cascades. Although

several mechanisms are likely to be involved in the TTA-mediated effects on growth, we propose that modulation of cellular redox conditions caused by changes in fatty acid metabolism may be of vital importance.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:757737 CAPLUS
DOCUMENT NUMBER: 134:95450
TITLE: Clofibrate pretreatment in mice confers resistance against hepatic lipid peroxidation
AUTHOR(S): Nicholls-Grzemski, Felicity A.; Belling, G. Brian; Priestly, Brian G.; Calder, Ian C.; Burcham, Philip C.
CORPORATE SOURCE: Molecular Toxicology Research Group, Department of Clinical and Experimental Pharmacology, University of Adelaide, Adelaide, 5005, Australia
SOURCE: Journal of Biochemical and Molecular Toxicology (2000), 14(6), 335-345
CODEN: JBMTFQ; ISSN: 1095-6670
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pretreatment with peroxisome proliferators protects mice against various hepatotoxicants. Since our previous work suggested that the hepatoprotection may involve an increased ability to cope with oxidative stress, the present work directly addressed this possibility. Several observations indicated a heightened defense against oxidative stress accompanies the hepatoprotection produced by clofibrate. Firstly, the carbonyl content of hepatic proteins from clofibrate-pretreated mice was 40% lower than those from vehicle-treated controls. Secondly, liver homogenates from clofibrate-pretreated mice produced less thiobarbituric acid reactive substances upon incubation under aerobic conditions or exposure to ferrous sulfate. This effect was not due to lower levels of peroxidn.-prone polyunsatd. fatty acids in clofibrate-treated livers. Thirdly, in vitro expts. indicated that the antioxidant factor in liver homogenates from clofibrate-pretreated mice was not glutathione. Rather, since it was inactivated by proteases and heat treatment, we concluded that a protein is involved. Collectively, our results suggest that a resistance to lipid peroxidn. develops in mouse liver during exposure to clofibrate. The identity of the putative antioxidant protein and its contribution to the protection against liver toxicity observed in this and other labs. awaits future investigation.
REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:160682 CAPLUS
DOCUMENT NUMBER: 133:13341
TITLE: Expression of the hydrogen peroxide-generating enzyme fatty acyl CoA oxidase activates NF-κB
AUTHOR(S): Li, Yixin; Tharappel, Job C.; Cooper, Simon; Glenn, Michelle; Glauert, Howard P.; Spear, Brett T.
CORPORATE SOURCE: Graduate Center for Toxicology, University of Kentucky, Lexington, KY, USA
SOURCE: DNA and Cell Biology (2000), 19(2), 113-120
CODEN: DCEBE8; ISSN: 1044-5498
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peroxisome proliferators are a class of hepatic carcinogens in rodents and have been proposed to act in part by increasing

oxidative stress. Fatty acyl CoA oxidase (FAO), which is highly induced by peroxisome proliferators, is the hydrogen peroxide-generating enzyme of the peroxisomal β-oxidation pathway. We previously showed that the treatment of rats and mice with the peroxisome proliferator ciprofibrate resulted in increased hepatic NF-κB activity and suggested that this effect may be secondary to the action of H2O2-generating enzymes. To test this possibility directly, we have determined whether transient overexpression of FAO, in the absence of peroxisome proliferators, leads to NF-κB activation. Here, we show that FAO overexpression in Cos-1 cells, in the presence of an H2O2-generating substrate, can activate a NF-κB regulated reporter gene. Electrophoretic mobility shift assays further demonstrated that FAO expression increases nuclear NF-κB DNA binding activity in a dose-dependent manner. The antioxidants vitamin E and catalase can inhibit this activation. These results indicate that FAO mediates, at least in part, peroxisome proliferator-induced NF-κB activation.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:10423 CAPLUS

DOCUMENT NUMBER: 132:203096

TITLE: Activation of nuclear factor-κB by the peroxisome proliferator ciprofibrate in H4IIEC3 rat hepatoma cells and its inhibition by the antioxidants N-acetylcysteine and vitamin E

AUTHOR(S): Li, Y.; Glauert, H. P.; Spear, B. T.

CORPORATE SOURCE: Graduate Center for Toxicology, University of Kentucky, Lexington, KY, USA

SOURCE: Biochemical Pharmacology (2000), 59(4), 427-434
CODEN: BCPCA6; ISSN: 0006-2952

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferators are a class of hepatic carcinogens in rodents and are proposed to act in part by increasing reactive oxygen species such as hydrogen peroxide. We previously showed that treatment of rats with ciprofibrate, a peroxisome proliferator, results in increased hepatic nuclear factor-κB (NF-κB) DNA binding activity. In this study, we have examined the link between peroxisome proliferators and NF-κB activation in hepatoma cell lines to test whether increased nuclear NF-κB levels activate NF-κB-regulated genes and to determine the mechanism of NF-κB activation. Electrophoretic mobility shift assays demonstrated NF-κB induction by ciprofibrate in peroxisome proliferator-responsive H4IIEC3 rat hepatoma cells but not in peroxisome proliferator-insensitive HepG2 human hepatoma cell lines. In addition, we found that stably transfected NF-κB-regulated reporter genes were activated by ciprofibrate in H4IIEC3 cells. This reporter gene activation was blocked by the antioxidants N-acetylcysteine and vitamin E. These studies suggest that hepatocytes are at least partially responsible for peroxisome proliferator-mediated hepatic NF-κB activation, and support the possibility that this activation is dependent upon reactive oxygen species.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:590120 CAPLUS

DOCUMENT NUMBER: 127:257568
ORIGINAL REFERENCE NO.: 127:50189a,50192a
TITLE: Antioxidant-mediated attenuation of the induction of cytochrome P450BM-3 (CYP102) by ibuprofen in Bacillus megaterium ATCC 14581
AUTHOR(S): English, Neil T.; Rankin, Lorna C.
CORPORATE SOURCE: SCHOOL OF APPLIED SCIENCES, THE ROBERT GORDON UNIVERSITY, ABERDEEN, AB25 1HG, UK
SOURCE: Biochemical Pharmacology (1997), 54(4), 443-450
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bacillus megaterium contains a soluble cytochrome P 450 termed BM-3, which is highly inducible by barbiturates, peroxisome proliferators, and nonsteroidal antiinflammatory drugs. In rats and mice, the chronic administration of peroxisome proliferators induces a sustained oxidative stress in hepatic tissue and may be responsible for the nongenotoxic carcinogenesis observed with prolonged treatment. Here it is shown that ibuprofen induces a variety of enzymes associated with the oxidative stress response in Bacillus, including catalase, glucose-6-phosphate-dehydrogenase, and aldehyde reductase in a dose-related manner. Furthermore, evidence is presented to show that the expression of cytochrome P 450 in Bacillus is associated with a marked depletion in cellular glutathione levels and that it renders these cells considerably more sensitive to oxidant insult. Finally, this work reports that a variety of structurally diverse antioxidants such as ascorbic acid, reduced glutathione, α-tocopherol acetate and the artificial antioxidant, butylated hydroxyanisole, all dramatically attenuate the expression of the cytochrome P450BM-3 gene and its repressor, Bm3R1, following ibuprofen treatment. These observations provide the first evidence that the expression of cytochrome P 450 genes can lead to increased oxidant sensitivity but can be strongly modulated by dietary and artificial antioxidants, as well as antioxidant enzymes. The important implications of this phenomenon are also discussed.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:273231 CAPLUS
DOCUMENT NUMBER: 126:338674
ORIGINAL REFERENCE NO.: 126:65699a,65702a
TITLE: Chemiluminescence and antioxidant levels during peroxisome proliferation by fenofibrate
AUTHOR(S): Lores Arnaiz, Silvia; Travacio, Marina; Monserrat, Alberto J.; Cutrin, Juan C.; Llesuy, Susana; Boveris, Alberto
CORPORATE SOURCE: National Laboratory of Free Radical Biology, School of Pharmacy and Biochemistry, University of Buenos Aires, Junin 956, Buenos Aires, 1113, Argent.
SOURCE: Biochimica et Biophysica Acta, Molecular Basis of Disease (1997), 1360(3), 222-228
CODEN: BBADEX; ISSN: 0925-4439
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fenofibrate, the hypolipidemic drug and peroxisome proliferator, was given to mice (0.23% weight/weight in the diet) during 1-3 wk and H2O2 and TBARS steady state concns., liver chemiluminescence and antioxidant levels were

measured. Administration of fenofibrate during 2 wk induced an increase of 89% in H2O2 steady state concentration Spontaneous chemiluminescence was decreased by 57% during fenofibrate treatment, while no significant effect was observed on TBARS concentration Hydroperoxide-initiated chemiluminescence was decreased by 56% after 15 days of fenofibrate treatment, probably due to an increase in endogenous antioxidant levels. Total and oxidized glutathione increased gradually after fenofibrate administration, obtaining maximal increases of 67% and 58% resp., after 22 days of treatment. An increase of 55% was found in ubiquinol levels in treated mice, as compared with the controls. α-tocopherol content was decreased by 51% in the liver of fenofibrate-treated mice. According to our findings, the high rate of H2O2 production associated with peroxisome proliferation, would not lead to an increase in lipid peroxidn. This can be explained by the presence of high levels of ubiquinols, which act as an antioxidant. The increased production of H2O2, would lead to DNA damage directly, and not through lipid peroxidn. processes.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:121874 CAPLUS
DOCUMENT NUMBER: 124:168043
ORIGINAL REFERENCE NO.: 124:31027a,31030a
TITLE: Oxidative stress in nongenotoxic carcinogenesis
AUTHOR(S): Klaunig, J. E.; Xu, Y.; Bachowski, S.; Ketcham, C. A.; Isenberg, J. S.; Kolaja, K. L.; Baker, T. K.; Walborg, E. F. Jr.; Stevenson, D. E.
CORPORATE SOURCE: Division of Toxicology, Department of Pharmacology and Toxicology, Indiana University School of Medicine, 1001 Walnut St., MF003, Indianapolis, IN, USA
SOURCE: Toxicology Letters (1995), 82/83(1-6), 683-91
CODEN: TOLED5; ISSN: 0378-4274
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The induction of oxidative stress in the target tissue has been proposed as a possible mechanism of action for nongenotoxic carcinogens. A variety of nongenotoxic hepatocarcinogens including peroxisome proliferators, organochlorines, barbiturates, and metals have been shown to produce an increase in reactive oxygen species (ROS) in the liver. The authors examined the induction of oxidative stress by the organochlorine mouse hepatic carcinogen, dieldrin. Using a salicylate spin trap assay, dieldrin produced mouse liver-specific increases in ROS in cultured hepatocytes. Increased amts. of hepatic 8-hydroxy-2'-deoxyguanosine and malondialdehyde (MDA) and decreased levels of cellular antioxidants were also seen in cultured mouse hepatocytes following dieldrin treatment. In subchronically dieldrin-treated mice and rats, hepatic vitamin E (Vit E) decrease was correlated with the dieldrin dose. While Vit E levels were decreased in both rats and mice, the normal lower levels of Vit E in the mouse resulted in a subsequent oxidative stress, evidenced by an increase in MDA formation in the mouse liver. Dieldrin also produced a dose-dependent increase in DNA synthesis in the mouse (not the rat) following subchronic treatment. These effects seen in both cells in culture and in vivo were species-specific, organ-specific, and dose-dependent which directly correlated with the observed pattern of cancer induction for dieldrin in rodents (mouse liver-specific). These findings support a possible role for the induction of oxidative stress in nongenotoxic hepatic carcinogenesis possibly through modulation of gene expression.

L12 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:643357 CAPLUS
DOCUMENT NUMBER: 119:243357
ORIGINAL REFERENCE NO.: 119:43231a,43234a
TITLE: Hepatomegaly is an early biomarker for hepatocarcinogenesis induced by peroxisome proliferators
AUTHOR(S): Takagi, Atsuya; Sai, Kimie; Umemura, Takashi; Hasegawa, Ryuichi; Kurokawa, Yuji
CORPORATE SOURCE: Div. Toxicol., Natl. Inst. Hyg. Sci., Tokyo, 158, Japan
SOURCE: Journal of Environmental Pathology, Toxicology and Oncology (1992), 11(3), 145-9
CODEN: JEPOEC; ISSN: 0731-8898
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relationship between hepatomegaly and the hepatocarcinogenesis associated with by peroxisome proliferators was examined Male F-344 rats were maintained on diets containing clofibrate, ciprofibrate, nafenopin, gemfibrozil, Wy-14, 643, di(2-ethylhexyl) phthalate (DEHP), or di(2-ethylhexyl) adipate (DEHA) at carcinogenic doses for 1 wk. A close correlation between relative liver wts. and hepatocarcinogenicity was observed (r = 0.910). Administration of perfluorooctanoic acid (PFOA), perfluorodecanoic acid (PFDA), simfibrate or DL-040, for which hepatocarcinogenicity is not know, resulted in hepatomegaly in all treated groups, this being especially marked in the PFOA case. Therefore, PFOA may have strong hepatocarcinogenic potential. Administration of the antioxidants BHA or vitamin E (VE) did not affect the hepatomegaly induced by DEHP. These results suggest that the hepatomegaly may be an early biomarker for prediction of the potential hepatocarcinogenicity of peroxisome proliferators. However, this requires further clarification in terms of its relation to the oxidative stress thought to be involved in peroxisome proliferator-induced hepatocarcinogenesis.

L12 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:205025 CAPLUS
DOCUMENT NUMBER: 118:205025
ORIGINAL REFERENCE NO.: 118:35009a,35012a
TITLE: Relationship between peroxisome-proliferating sulfur-substituted fatty acid analogs, hepatic lipid peroxidation and hydrogen peroxide metabolism
AUTHOR(S): Demoz, Abraham; Svardal, Asbjoern; Berge, Rolf Kristian
CORPORATE SOURCE: Inst. Clin. Biol., Univ. Bergen, Bergen, N-5021, Norway
SOURCE: Biochemical Pharmacology (1993), 45(1), 257-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of the administration of three peroxisome-proliferating sulfur-substituted fatty acid analogs on hepatic antioxidant status and lipid peroxidn. was studied in rats. After 14 days of treatment, the ratio of induction of peroxisomal fatty acyl-CoA oxidase to catalase was 4.2 and 3.5 in rats treated with 1,10-bis-(carboxymethylthio)decane (BCMTD) and 1-mono(carboxymethylthio)tetradecane (CMTTD), resp., while the corresponding ratio was 1.3 in 1-mono(carboxyethylthio)tetradecane (CETTD)-treated rats. As compared to the controls, an increase in hepatic

hydrogen peroxide content was noted in BCMTD- and CMTTD-treated rats, but not CETTD-treated rats. Hepatic lipid peroxidn. was increased in all the three treatment groups in a manner not related to the potency of the compds. to induce the peroxisomal hydrogen peroxide metabolizing enzymes. Hepatic glutathione content increased while the activities of its associated enzymes such as glutathione transferase, glutathione peroxidase and glutathione reductase decreased in all the treated rats. Taken together, these data show a relationship between the levels of hydrogen peroxide and lipid peroxidn. in rat livers treated with BCMTD and CMTTD. However, increased hepatic lipid peroxidn. in CETTD-treated rats cannot be accounted for by the changes in the peroxisomal enzymes.

L12 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:207629 CAPLUS
DOCUMENT NUMBER: 116:207629
ORIGINAL REFERENCE NO.: 116:34959a,34962a
TITLE: Effects of the peroxisome proliferators ciprofibrate and perfluorodecanoic acid on hepatic cellular antioxidants and lipid peroxidation in rats
AUTHOR(S): Glauert, Howard P.; Srinivasan, Suseela; Tatum, Vickie L.; Chen, Li Chuan; Saxon, Danita M.; Lay, L. Travis; Borges, Tim; Baker, Michael; Chen, Linda H.; et al.
CORPORATE SOURCE: Dep. Nutr. Food Sci., Univ. Kentucky, Lexington, KY, 40506, USA
SOURCE: Biochemical Pharmacology (1992), 43(6), 1353-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to determine if hepatic cellular antioxidants and indexes of oxidative damage are altered by administration of the peroxisome proliferators ciprofibrate and perfluorodecanoic acid (PFDA). Rats were fed 0.01% ciprofibrate in the diet or were injected with PFDA (0.5 or 5.0 mg/kg, i.p.) every 4 wk for 6, 14, 30, 54, and 78 wk. Peroxisomal fatty acyl-CoA oxidase and catalase activities were increased by both ciprofibrate and PFDA throughout the study. Neither ciprofibrate nor PFDA increased the levels of malonaldehyde or conjugated dienes, but ciprofibrate decreased these indexes at early time points. Ciprofibrate decreased the following cellular antioxidants or antioxidant enzymes: vitamin C, vitamin D, DT-diaphorase, glutathione peroxidase, glutathione-S-transferase, and glutathione reductase; superoxide dismutase and glutathione were not affected. PFDA decreased DT-diaphorase and increased superoxide dismutase, but did not affect other cellular antioxidants. This study shows that administration of the peroxisome proliferators ciprofibrate and PFDA did not increase indexes of lipid peroxidn., but that cellular antioxidant defenses were inhibited for a prolonged period of time by the peroxisome proliferator ciprofibrate.

L12 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:673165 CAPLUS
DOCUMENT NUMBER: 115:273165
ORIGINAL REFERENCE NO.: 115:46257a,46260a
TITLE: Analysis of the effects of modifying agents on proliferation and enzyme phenotype in focal preneoplastic and neoplastic liver lesions in rats
AUTHOR(S): Tsuda, H.; Ozaki, K.; Uwagawa, S.; Takahashi, S.; Hakoi, K.; Kato, T.; Fukushima, S.; Sato, K.; Ito, N.
CORPORATE SOURCE: Sch. Med., Fujita Health Univ., Toyoake, 470-11, Japan
SOURCE: Chem. Carcinog. 2, [Proc. Sardinian Int. Meet.

Modulating Factors Multistage Chem. Carcinog.], 5th (1991), Meeting Date 1989, 219-29. Editor(s): Columbano, Amedeo. Plenum: New York, N. Y.
CODEN: 57LMAZ
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The markers analyzed were glutathione S-transferase placental form (GST-P), glucose-6-phosphate dehydrogenase (G6PD), glucose 6-phosphate, ATPase and gamma glutamyltranspeptidase and incorporation of 5-bromo-2-deoxyuridine being used to assess DNA synthesis levels. After initiation with DEN F344 rats were subsequently administered the hepatocarcinogen 2-acetylaminofluorene (2-AAF, 0.01%), the hepatopromoter Na phenobarbital (PB, 0.05%), the antioxidant inhibitors ethoxyquin (0.5%) or BHA, 1%, or the peroxisome proliferators DEHP (0.3%) or clofibrate (1%). Sacrifice at the 16 and 32 wk time points after partial hepatectomy performed at week 3 revealed that the 2-AAF and PB promoting regimens were associated with increased conformity in marker expression especially in more rapidly growing lesions, where three or even four enzymes were changed in concert. The antioxidant inhibitory agents, in contrast, brought about a decrease so that the single or double alteration phenotype was the most commonly observed Focal populations in the peroxisomal proliferator cases were characterized by an almost complete dissociation of proliferative status from degree of conformity. The results also suggested clear differential in the ability of markers to differentiate putative preneoplastic lesions dependent on treatment conditions. Overall GST-P was the most reliable although G6PD was most accurate in the peroxisome proliferator cases.

L12 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:153439 CAPLUS
DOCUMENT NUMBER: 112:153439
ORIGINAL REFERENCE NO.: 112:25807a,25810a
TITLE: Peroxisome proliferator-induced alterations in the expression and modification of rat hepatocyte plasma membrane proteins
AUTHOR(S): Bartles, James R.; Khuon, Satya; Lin, Xuanhui; Zhang, Liqin; Reddy, Janardan K.; Rao, M. Sambasiva; Isoye, Steven T.; Nehme, Cheryl L.; Fayos, Barbara E.
CORPORATE SOURCE: Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA
SOURCE: Cancer Research (1990), 50(3), 669-76
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rats were fed the peroxisome proliferator ciprofibrate (0.025%), and the effects on the expression, modification, and localization of seven domain-specific integral proteins of the rat hepatocyte plasma membrane were assessed using a combination of immunoblotting,-precipitation, and -fluorescence. Ciprofibrate caused the down-regulation of five of the plasma membrane proteins (the epidermal growth factor receptor, the asialoglycoprotein receptor, HA321, HA 4, and dipeptidylpeptidase IV) and induced the expression of a more basic, lower-M, isoform of the basolateral plasma membrane protein CE 9. Pulse labeling, chemical deglycosylation, and 125I-labeled wheat germ lectin blotting suggested that the ciprofibrate-induced isoform of CE 9 differed in the posttranslational modification of its oligosaccharides and contained more sialic acid. These changes in hepatocyte surface differentiation were first observed between days 1 and 5 on the ciprofibrate-containing diet, coincident with other aspects of the pleiotropic response of the hepatocyte to peroxisome proliferators, e.g., the induction of the Mr 78,000 peroxisome proliferation-associated protein. The effects were reversed within 2-3 wk upon removal of ciprofibrate. The

three other peroxisome proliferators tested, bis(2-ethylhexyl) phthalate, clofibrate, and Wy 14,643, exerted most of the same effects on the expression and modification of the hepatocyte plasma membrane proteins, but the compds. differed in relative potency. The ciprofibrate-induced decreases in the concns. of the epidermal growth factor receptor, the asialoglycoprotein receptor, HA 321, and HA 4 were similar to the selective down-regulation of these proteins observed transiently during the period of hepatocyte proliferation following two-thirds hepatectomy. Other compds. frequently used in studies of liver enzyme induction and carcinogenesis, the antioxidants ethoxyquin and butylated hydroxyanisole and the liver tumor promoter phenobarbital, were not as effective as ciprofibrate or two-thirds hepatectomy at causing the down-regulation of these proteins. The induction of the lower-M, isoform of the basolateral plasma membrane protein CE 9 was not observed following two-thirds hepatectomy or upon the feeding of the antioxidants or phenobarbital but was specific to the feeding of the peroxisome proliferators.

L12 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:62796 CAPLUS
DOCUMENT NUMBER: 106:62796
ORIGINAL REFERENCE NO.: 106:10271a
TITLE: Mitogenicity of peroxisome proliferators in monolayers of adult rat hepatocytes
AUTHOR(S): Bieri, F.; Bentley, P.; Waechter, F.; Staeubli, W.
CORPORATE SOURCE: Cent. Toxicol. Unit, Ciba-Geigy Ltd., Basel, 4002, Switz.
SOURCE: Food and Chemical Toxicology (1986), 24(6-7), 709
CODEN: FCTOD7; ISSN: 0278-6915
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The induction of peroxisomal enzymes and of replicative DNA synthesis were studied to examine the possible interrelation between these effects and to classify their importance in the carcinogenic process. The time course and reversibility of both effects were superimposable, but the dose response differed, being linear ≤100 μg/mL for peroxisomal enzyme induction, and showing a maximum at 10 μg/mL for induction of DNA synthesis. Several substances (e.g., prostaglandin synthesis inhibitors and antioxidants) were added to the culture medium to alter either replicative DNA synthesis or the oxidative effects resulting from peroxisome proliferation. The 2 parameters seemed to be altered independently, providing no evidence of any direct correlation. Dose-response curves with known peroxisome proliferators and related compds. indicated that the mitogenic potency of the proliferators could not be predicted from their effects on the peroxisomal compartment. Ranking of the substances according to their ability to induce replicative DNA synthesis in cultured hepatocytes was more in agreement with their hepatomegalic potency than was their ranking as peroxisome proliferators. The mitogenic potency of the substance and the peroxisome proliferation should be measured when the monolayers of adult rat hepatocytes are used to assess the possible hepatocarcinogenicity of the test substances.

L12 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:73924 CAPLUS
DOCUMENT NUMBER: 102:73924
ORIGINAL REFERENCE NO.: 102:11515a,11518a
TITLE: Prooxidant states and tumor promotion
AUTHOR(S): Cerutti, Peter A.

CORPORATE SOURCE: Dep. Carcinog., Swiss Inst. Exp. Cancer Res., Epalinges, CH-1066, Switz.
SOURCE: Science (Washington, DC, United States) (1985), 227(4685), 375-81
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is convincing evidence that cellular prooxidant states-i.e., increased concns. of active O and organic peroxides and radicals-can promote initiated cells to neoplastic growth. Prooxidant states can be caused by different classes of agents, including hyperbaric O, radiation, xenobiotic metabolites and Fenton-type reagents, modulators of the cytochrome P 450 electron-transport chain, peroxisome proliferators, inhibitors of the antioxidant defense, and membrane-active agents. Many of these agents are promoters or complete carcinogens. They cause chromosomal damage by indirect action, but the role of this damage in carcinogenesis remains unclear. Prooxidant states can be prevented or suppressed by the enzymes of the cellular antioxidant defense and low mol. weight scavenger mols., and many antioxidants are antipromoters and anticarcinogens. Finally, prooxidant states may modulate the expression of a family of prooxidant genes, which are related to cell growth and differentiation, by inducing alterations in DNA structure or by epigenetic mechanisms, for example, by polyadenosine diphosphate-ribosylation of chromosomal proteins.

L12 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1983:172753 CAPLUS
DOCUMENT NUMBER: 98:172753
ORIGINAL REFERENCE NO.: 98:26053a,26056a
TITLE: Noninhibitory effect of antioxidants ethoxyquin, 2(3)-tert-butyl-4-hydroxyanisole and 3,5-di-tert-butyl-4-hydroxytoluene on hepatic peroxisome proliferation and peroxisomal fatty acid β-oxidation induced by a hypolipidemic agent in rats
AUTHOR(S): Lalwani, Narendra D.; Reddy, M. Kumudavalli; Qureshi, Saeed A.; Moehle, Charles M.; Hayashi, Hidenori; Reddy, Janardan K.
CORPORATE SOURCE: Med. Sch., Northwestern Univ., Chicago, IL, 60611, USA
SOURCE: Cancer Research (1983), 43(4), 1680-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The acute effects of antioxidants ethoxyquin [91-53-2], 2(3)-tert-butyl-4-hydroxyanisole [25013-16-5], and 3,5-di-tert-butyl-4-hydroxytoluene [128-37-0] on hepatocarcinogenesis by peroxisome proliferators such as ciprofibrate [52214-84-3] were studied in rats. Ethoxyquin at 0.5% (weight/weight) dietary level exerted no inhibitory effect on the induction by ciprofibrate (0.1%, weight/weight) of hepatomegaly, peroxisome proliferation (volume and numerical d.), catalase, carnitine acetyltransferase, heat-labile peroxisomal enoyl-CoA hydratase, and the peroxisomal fatty acid β-oxidation system. Both 2(3)-tert-butyl-4-hydroxyanisole (0.7%, weight/weight) and 3,5-di-tert-butyl-4-hydroxytoluene (0.7
or 0.07%) also failed to inhibit the ciprofibrate-induced hepatomegaly and hepatic peroxisome proliferation. Addnl., none of these antioxidants altered the ciprofibrate-induced increase in Mr 80,000 peroxisome proliferation-associated polypeptide in liver. The similar increases in peroxisome population and elevations of H2O2-producing peroxisomal fatty acid β-oxidation system suggest that excess levels of intracellular H2O2 are generated in the livers of rats fed ciprofibrate

either alone or in combination with a dietary antioxidant. These expts. provide a model system to test the hypothesis that peroxisome proliferator carcinogenesis is mediated by H2O2 and that antioxidants by inhibiting lipid peroxidn. could retard or inhibit this process.

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     (FILE 'HOME' ENTERED AT 23:21:40 ON 27 JUN 2008)

     FILE 'REGISTRY' ENTERED AT 23:21:50 ON 27 JUN 2008
               E ROSIGLITAZONE
L1             9 S E3
               E "COENZYME Q10"

     FILE 'CAPLUS' ENTERED AT 23:23:04 ON 27 JUN 2008
L2            92 S L1 AND ANTIOXIDANT
L3             4 S L2 AND "COENZYME Q10"
L4            22 S L2 AND 1960<=PY<=2003
L5            22 DUP REM L4 (0 DUPLICATES REMOVED)
               E PPAR AGONISTS+ALL/CT
L6          2471 S (PPAR AGONISTS OR "PEROXISOME PROLIFERATORS")
L7          2471 S ("PPAR AGONISTS" OR "PEROXISOME PROLIFERATORS")
L8           266 S L7 AND OBESITY
L9            24 S L8 AND 1960<=PY<=2003
L10       118753 S ANTIOXIDANTS
L11          117 S L7 AND L10
L12           30 S L11 AND 1960<=PY<=2003

=> s L10 and obesity
          50960 OBESITY
             85 OBESITIES
          50963 OBESITY
                (OBESITY OR OBESITIES)
L13         564 L10 AND OBESITY

=> S L13 AND 1960<=PY<=2003
       21227234 1960<=PY<=2003
L14         134 L13 AND 1960<=PY<=2003

=> s L14 and L7
L15           4 L14 AND L7

=> d l15 1-4 ibib ab

L15  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2003:991491  CAPLUS
DOCUMENT NUMBER:          140:27832
TITLE:                    Preparation of triazolyl 11β-hydroxysteroid
                          dehydrogenase-1 inhibitors for the treatment of
                          diabetes, obesity and dyslipidemia
INVENTOR(S):              Olson, Steven H.; Balkovec, James M.; Zhu, Yuping
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 144 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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WO 2003104208	A1	20031218	WO 2003-US17890	20030606 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2488592	A1	20031218	CA 2003-2488592	20030606 <--
AU 2003251410	A1	20031222	AU 2003-251410	20030606 <--
EP 1532122	A1	20050525	EP 2003-757385	20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1659151	A	20050824	CN 2003-813392	20030606
CN 1990474	A	20070704	CN 2007-10003770	20030606
US 20040048912	A1	20040311	US 2003-457682	20030609
US 6730690	B2	20040504		
US 20040106664	A1	20040603	US 2003-697547	20031030
US 7179802	B2	20070220		
ZA 2004008772	A	20051118	ZA 2004-8772	20041029
PRIORITY APPLN. INFO.:			US 2002-387385P	P 20020610
			CN 2003-813392	A3 20030606
			WO 2003-US17890	W 20030606
			US 2003-457682	A3 20030609

OTHER SOURCE(S): MARPAT 140:27832

AB Title compds. I [A = halo, alkyl, Ph, etc.; B = H, halo, alkyl, S-alkyl, etc. or A, B = taken together are (un)substituted alkylene; R1 = H, OH, halo, alkyl, alkoxy, aryl, etc.; R2 = alkyl, alkoxy, Ph, etc.; R3 = alkyl, alkenyl, thioalkoxy, aryl, heterocyclyl, etc. or R2-3 = taken together fused 5-6-membered alkyl/aryl ring] are prepared For instance, 2,2-diphenylbutanoic acid is converted to the corresponding hydrazide (DMF, Et3N, TFFH, H2NNH2, 0°, 30 min). 8-Methoxy-2,3,4,5,6,7-hexahydroazocine is then reacted with the intermediate (DMF, 120°, overnight) to give II. Example compds. exhibit IC50 < 500 nM for 11β-hydroxysteroid dehydrogenase-1 (11β-HSD1). I are useful for the treatment of diabetes, such as noninsulin-dependent diabetes (NIDDM), hyperglycemia, obesity, insulin resistance, dylsipidemia, hyperlipidemia, hypertension, Syndrome X and other symptoms associated with NIDDM.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:637640 CAPLUS
DOCUMENT NUMBER: 137:185320
TITLE: PPAR agonists, e.g., 3-[4-[2-[3-(2,4-dimethoxyphenyl)-1-heptylureido]ethyl]phenyl]-2-ethoxypropionic acid and analogs, useful particularly as PPARα agonists, and their pharmaceutical compositions and therapeutic use as hypolipemics, antidiabetics, etc.
INVENTOR(S): Hayward, Cheryl Myers; Perry, David Austen
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064549	A1	20020822	WO 2002-IB45	20020107 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2438551	A1	20020822	CA 2002-2438551	20020107 <--
AU 2002216330	A1	20020828	AU 2002-216330	20020107 <--
EP 1360172	A1	20031112	EP 2002-740089	20020107 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002007285	A	20040210	BR 2002-7285	20020107
JP 2004529097	T	20040924	JP 2002-564482	20020107
US 20020165282	A1	20021107	US 2002-76740	20020214 <--
US 6699904	B2	20040302		
MX 2003PA07284	A	20031204	MX 2003-PA7284	20030814 <--
PRIORITY APPLN. INFO.:			US 2001-269058P P	20010215
			WO 2002-IB45 W	20020107

OTHER SOURCE(S): MARPAT 137:185320

AB Title compds. I and their prodrugs and/or pharmaceutically acceptable salts are claimed [wherein: E = CO, SO2; B = CH2, NH; Z = CO2H, CHO, CH2OH, alkoxycarbonyl, cyano, CONHOH, tetrazolyl, tetrazolylaminocarbonyl, 4,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl, 3-oxo-isoxazolidin-4-ylaminocarbonyl, CONHSO2R4; R1 = H, alkyl, cycloalkyl; R2 = H, cycloalkyl, (un)substituted and/or (un)saturated (hetero)aliphatic chain; R3 = (un)substituted alk(en/yn)yl; R4 = alkyl, amino or its (di)((poly)fluoro)alkyl derivs.; R5, R6 = H, alkyl, cycloalkyl, or cycloalkylalkyl; or R5R6 = atoms to form 3- to 6-membered fully saturated carbocyclic ring; A = H, (di)(alkyl)amino, alkanoylamino, alkoxy, or (un)substituted (un)saturated (bi)(hetero)cyclic ring; W = bond, NH, N-alkyl, alkylamino (sic), or alkylene; or W = CR7R8 where R7R8 = atoms to form 3- to 6-membered fully saturated carbocyclic ring]. The compds. are disclosed as PPAR (peroxisome proliferator-activated receptor) agonists, and particularly as PPARα activators (no data). Also disclosed are pharmaceutical compns. containing I, and the use of I to elevate certain plasma lipid levels, including high d. lipoprotein-cholesterol, and to lower certain other plasma lipid levels, such as LDL-cholesterol and triglycerides, and accordingly to treat diseases which are exacerbated by low levels of HDL cholesterol and/or high levels of LDL-cholesterol and triglycerides, such as atherosclerosis and cardiovascular diseases, in mammals, including humans. Further claimed uses include treatment of obesity, diabetes and related conditions, atherosclerosis, hypertension, inflammation, and thrombosis. The compds. may also be administered in combination with a variety of other enzyme inhibitors. A total of 77 synthetic examples cover production of various I and their intermediates. The (R)- and (S)-enantiomers of approx. 15 compds. are specifically claimed. For instance, [4-(2-heptylaminoethyl)phenyl]methano l (preparation in 3 steps given) underwent a sequence of: (1) N-protection with BOC, (2) O-oxidation with MnO2 to an aldehyde, (3) Wittig type reaction of the latter with Ph2P(:O)CH(OEt)CO2Et, (4) reduction of the resultant acrylate ester to a propionate ester, (5) removal of BOC, (6) carbamoylation with 2,4-dimethoxyphenyl isocyanate, and (7) alkaline hydrolysis of the Me ester,

to give title compound II.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:575765 CAPLUS
DOCUMENT NUMBER: 137:140435
TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of diabetes and lipid disorders, and their preparation, pharmaceutical compositions, and use
INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20020103242	A1	20020801	US 2001-21667	20011029	<--
US 6713508	B2	20040330			
CA 2427610	A1	20020808	CA 2001-2427610	20011026	<--
WO 2002060434	A2	20020808	WO 2001-US49501	20011026	<--
WO 2002060434	A3	20030619			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002248221	A1	20020812	AU 2002-248221	20011026	<--
AU 2002248221	B2	20060817			
EP 1347755	A2	20031001	EP 2001-997102	20011026	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004517938	T	20040617	JP 2002-560626	20011026	
PRIORITY APPLN. INFO.:			US 2000-244698P	P 20001031	
			WO 2001-US49501	W 20011026	

OTHER SOURCE(S): MARPAT 137:140435
AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms (un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs.,

alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their preparation is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alkaline hydrolysis (100%), to give title compound II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a number of specific drugs, is claimed.

L15 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:617987 CAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and lipid disorders
INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
PATENT ASSIGNEE(S): Merck & Co. Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2400021	A1	20010823	CA 2001-2400021	20010214 <--
AU 2001038214	A5	20010827	AU 2001-38214	20010214 <--
AU 784722	B2	20060601		
EP 1259494	A1	20021127	EP 2001-910624	20010214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523336	T	20030805	JP 2001-560192	20010214 <--

PRIORITY APPLN. INFO.: US 2000-183593P P 20000218
WO 2001-US4636 W 20010214

OTHER SOURCE(S): MARPAT 135:180757
AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prepared For example, 2,4-dihydroxy-3,5-dipropyl-

1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me α-bromoisobutyrate in the presence of Cs2CO3 in DMF, followed by saponification, afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) α and/or γ and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPARα and/or γ mediated diseases, disorders, and conditions (no data).
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 23:21:40 ON 27 JUN 2008)

FILE 'REGISTRY' ENTERED AT 23:21:50 ON 27 JUN 2008
E ROSIGLITAZONE
L1 9 S E3
E "COENZYME Q10"

FILE 'CAPLUS' ENTERED AT 23:23:04 ON 27 JUN 2008
L2 92 S L1 AND ANTIOXIDANT
L3 4 S L2 AND "COENZYME Q10"
L4 22 S L2 AND 1960<=PY<=2003
L5 22 DUP REM L4 (0 DUPLICATES REMOVED)
E PPAR AGONISTS+ALL/CT
L6 2471 S (PPAR AGONISTS OR "PEROXISOME PROLIFERATORS")
L7 2471 S ("PPAR AGONISTS" OR "PEROXISOME PROLIFERATORS")
L8 266 S L7 AND OBESITY
L9 24 S L8 AND 1960<=PY<=2003
L10 118753 S ANTIOXIDANTS
L11 117 S L7 AND L10
L12 30 S L11 AND 1960<=PY<=2003
L13 564 S L10 AND OBESITY
L14 134 S L13 AND 1960<=PY<=2003
L15 4 S L14 AND L7

=> s L7 and "Vitamin E"
210581 "VITAMIN"
60075 "VITAMINS"
233974 "VITAMIN"
("VITAMIN" OR "VITAMINS")
2136546 "E"
38842 "VITAMIN E"
("VITAMIN"(W)"E")
L16 22 L7 AND "VITAMIN E"

=> S L16 AND 1960<=PY<=2003
21227234 1960<=PY<=2003
L17 11 L16 AND 1960<=PY<=2003

=> d L17 1-11 ibib ab

L17 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:620087 CAPLUS
DOCUMENT NUMBER: 147:16717
TITLE: Progenitor endothelial cell capturing with a

drug-eluting implantable medical device

INVENTOR(S): Cottone, Robert John, Jr.; Rowland, Stephen M.; Parker, Sherry

PATENT ASSIGNEE(S): Orbusneich Medical, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 47pp., Cont.-in-part of U.S. Ser. No. 76,731.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 13

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 20070129789	A1	20070607	US 2006-561730	20061120	
US 20020049495	A1	20020425	US 2001-808867	20010315	<--
US 7037332	B2	20060502			
US 20030229393	A1	20031211	US 2003-360567	20030206	<--
WO 2003099169	A1	20031204	WO 2003-US15811	20030520	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003241515	A1	20031212	AU 2003-241515	20030520	<--
US 20040039441	A1	20040226	US 2003-442669	20030520	
CN 1655738	A	20050817	CN 2003-811531	20030520	
JP 2005525911	T	20050902	JP 2004-506697	20030520	
US 20050271701	A1	20051208	US 2005-76731	20050310	
US 20070134290	A1	20070614	US 2006-494801	20060726	
US 20070156232	A1	20070705	US 2006-562931	20061122	

PRIORITY APPLN. INFO.:

US 2000-189674P	P	20000315
US 2000-201789P	P	20000504
US 2001-808867	A2	20010315
US 2002-354680P	P	20020206
US 2002-382095P	P	20020520
US 2003-360567	A2	20030206
US 2003-442669	B2	20030520
US 2004-551978P	P	20040310
US 2005-76731	A2	20050310
US 2006-822451P	P	20060815
WO 2003-US15811	W	20030520
US 2004-832106	A1	20040426

AB A medical device for implantation into vessels or luminal structures within the body is provided, which stimulates pos. blood vessel remodeling. The medical device, such as a stent and a synthetic graft, is coated with a pharmaceutical composition consisting of a controlled-release matrix and one or more pharmaceutical substances for direct delivery of drugs to surrounding tissues. The coating on the medical device further comprises a ligand such as a peptide, an antibody or a small mol. for capturing progenitor endothelial cells in the blood contacting surface of the device for restoring an endothelium at the site of injury. In particular, the drug-coated stents are for use, for example, in balloon angioplasty procedures for preventing or inhibiting restenosis.

ACCESSION NUMBER: 2005:1004266 CAPLUS
DOCUMENT NUMBER: 143:299112
TITLE: Apolipoprotein or serum amyloid A-derived helical synthetic peptides that stimulate cellular cholesterol efflux for therapeutic use
INVENTOR(S): Bielicki, John K.; Natarajan, Pradeep
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 74 pp., Cont.-in-part of U.S. Ser. No. 142,238.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050202532	A1	20050915	US 2004-14187	20041215
US 20030087819	A1	20030508	US 2002-142238	20020508 <--
US 7217785	B2	20070515		

PRIORITY APPLN. INFO.:

US 2002-142238	A2	20020508
US 2003-529933P	P	20031215
US 2001-289944P	P	20010509

AB The present invention provides peptides comprising at least one amphipathic alpha helix and having a cholesterol mediating activity and an ATP-binding cassette transporter A (ABCA) stabilization activity. The peptide may be a fragment of an apolipoprotein or serum amyloid A. The peptides have antioxidant and anti-inflammatory activity and may be used with other therapeutic agents for treating cardiovascular disease.

L17 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:160682 CAPLUS
DOCUMENT NUMBER: 133:13341
TITLE: Expression of the hydrogen peroxide-generating enzyme fatty acyl CoA oxidase activates NF-κB
AUTHOR(S): Li, Yixin; Tharappel, Job C.; Cooper, Simon; Glenn, Michelle; Glauert, Howard P.; Spear, Brett T.
CORPORATE SOURCE: Graduate Center for Toxicology, University of Kentucky, Lexington, KY, USA
SOURCE: DNA and Cell Biology (2000), 19(2), 113-120
CODEN: DCEBE8; ISSN: 1044-5498
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peroxisome proliferators are a class of hepatic carcinogens in rodents and have been proposed to act in part by increasing oxidative stress. Fatty acyl CoA oxidase (FAO), which is highly induced by peroxisome proliferators, is the hydrogen peroxide-generating enzyme of the peroxisomal β-oxidation pathway. We previously showed that the treatment of rats and mice with the peroxisome proliferator ciprofibrate resulted in increased hepatic NF-κB activity and suggested that this effect may be secondary to the action of H2O2-generating enzymes. To test this possibility directly, we have determined whether transient overexpression of FAO, in the absence of peroxisome proliferators, leads to NF-κB activation. Here, we show that FAO overexpression in Cos-1 cells, in the presence of an H2O2-generating substrate, can activate a NF-κB regulated reporter gene. Electrophoretic mobility shift assays further demonstrated that FAO expression increases nuclear NF-κB DNA binding activity in a dose-dependent manner. The antioxidants vitamin E and catalase can inhibit this activation. These results

indicate that FAO mediates, at least in part, peroxisome proliferator-induced NF-κB activation.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:10423 CAPLUS
DOCUMENT NUMBER: 132:203096
TITLE: Activation of nuclear factor-κB by the peroxisome proliferator ciprofibrate in H4IIEC3 rat hepatoma cells and its inhibition by the antioxidants N-acetylcysteine and vitamin E
AUTHOR(S): Li, Y.; Glauert, H. P.; Spear, B. T.
CORPORATE SOURCE: Graduate Center for Toxicology, University of Kentucky, Lexington, KY, USA
SOURCE: Biochemical Pharmacology (2000), 59(4), 427-434
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peroxisome proliferators are a class of hepatic carcinogens in rodents and are proposed to act in part by increasing reactive oxygen species such as hydrogen peroxide. We previously showed that treatment of rats with ciprofibrate, a peroxisome proliferator, results in increased hepatic nuclear factor-κB (NF-κB) DNA binding activity. In this study, we have examined the link between peroxisome proliferators and NF-κB activation in hepatoma cell lines to test whether increased nuclear NF-κB levels activate NF-κB-regulated genes and to determine the mechanism of NF-κB activation. Electrophoretic mobility shift assays demonstrated NF-κB induction by ciprofibrate in peroxisome proliferator-responsive H4IIEC3 rat hepatoma cells but not in peroxisome proliferator-insensitive HepG2 human hepatoma cell lines. In addition, we found that stably transfected NF-κB-regulated reporter genes were activated by ciprofibrate in H4IIEC3 cells. This reporter gene activation was blocked by the antioxidants N-acetylcysteine and vitamin E. These studies suggest that hepatocytes are at least partially responsible for peroxisome proliferator-mediated hepatic NF-κB activation, and support the possibility that this activation is dependent upon reactive oxygen species.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:241838 CAPLUS
DOCUMENT NUMBER: 128:318256
ORIGINAL REFERENCE NO.: 128:62980h,62981a
TITLE: Toxic effect of systemic administration of low doses of the plasticizer di-(2-ethyl hexyl) phthalate [DEHP] in rats
AUTHOR(S): Nair, K. G. Padmakumaran; Deepadevi, K. V.; Arun, P.; Kumar, V. Manoj; Santhosh, Anitha; Lekshmi, L. R.; Kurup, P. A.
CORPORATE SOURCE: Department of Biological Sciences, Peninsula Polymers Limited, Trivandrum, 695 010, India
SOURCE: Indian Journal of Experimental Biology (1998), 36(3), 264-272
CODEN: IJEBA6; ISSN: 0019-5189
PUBLISHER: National Institute of Science Communication, CSIR
DOCUMENT TYPE: Journal

LANGUAGE: English

AB DEHP [di - (2 Et hexyl) phthalate], a widely used plasticizer in blood storage bags, leaches out in appreciable amts. into blood (about 10 mg / 100 mL) resulting in exposure of recipients of blood transfusion to this compound Various reports indicate the toxicity of DEHP, particularly in liver and reproductive organs but all these studies used large doses (up to 2g or more/Kg body weight) and oral route of administration which are not relevant to the i.v. administration during blood transfusion or the low amts. present in blood. The authors have studied changes in the activity of some important enzymes-γ-GT, ALT, CPK, LDH, alkaline phosphatase, acid phosphatase, β-glucuronidase and few other parameters like vitamin E, glutathione, serum albumin etc in rats administered low doses of DEHP (corresponding to transfusion of 2,4,6 and 10 units of blood). Histopathol. of the organs has also been carried out. The results obtained indicate no serious toxic effects for DEHP at the level present in blood stored in DEHP plasticized blood bags as evidenced by the lack of any significant alteration in most of the biochem. parameters studied. Even in those cases where there was alteration (e.g. decrease in the level of vitamin E) 24 h after administration of DEHP, it returned to near normal level with in 72 h to 7 days. No histopathol. changes were observed in any of the organs at these levels of DEHP. It is concluded that DEHP did not cause any serious toxic effect even at doses corresponding to transfusion of several units of blood in a recipient.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:202992 CAPLUS

DOCUMENT NUMBER: 126:208423

ORIGINAL REFERENCE NO.: 126:40217a,40220a

TITLE: Relationship of peroxisome proliferation-related biochemical changes to the hepatocarcinogenicity of the plasticizer di(2-ethylhexyl) phthalate

AUTHOR(S): Nagini, S.; Viswanathan, P.; Selvam, S.

CORPORATE SOURCE: Department of Biochemistry, Annamalai University, Annamalainagar, 608 002, India

SOURCE: Medical Science Research (1997), 25(2), 127-128
CODEN: MSCREJ; ISSN: 0269-8951

PUBLISHER: Chapman & Hall

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Di(2-ethylhexyl) phthalate (DEHP), a commonly used plasticizer, induces peroxisome proliferation and hepatocellular carcinomas in rodents on long-term exposure. The authors examined DEHP-induced biochem. changes that can be correlated with peroxisome proliferation and carcinogenicity. Hepatocellular carcinomas were induced following the continuous administration of DEHP for 96 wk. Rats fed DEHP showed enhanced hepatic lipid peroxidn., with a concomitant increase in ATPase activity. The levels of vitamin E and ascorbic acid declined significantly in animals treated with DEHP as compared to controls. These changes may contribute to the carcinogenic potential of peroxisome proliferators.

L17 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:121874 CAPLUS

DOCUMENT NUMBER: 124:168043

ORIGINAL REFERENCE NO.: 124:31027a,31030a

TITLE: Oxidative stress in nongenotoxic carcinogenesis

AUTHOR(S): Klaunig, J. E.; Xu, Y.; Bachowski, S.; Ketcham, C. A.;

Isenberg, J. S.; Kolaja, K. L.; Baker, T. K.; Walborg, E. F. Jr.; Stevenson, D. E.

CORPORATE SOURCE: Division of Toxicology, Department of Pharmacology and Toxicology, Indiana University School of Medicine, 1001 Walnut St., MF003, Indianapolis, IN, USA

SOURCE: Toxicology Letters (1995), 82/83(1-6), 683-91
CODEN: TOLED5; ISSN: 0378-4274
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The induction of oxidative stress in the target tissue has been proposed as a possible mechanism of action for nongenotoxic carcinogens. A variety of nongenotoxic hepatocarcinogens including peroxisome proliferators, organochlorines, barbiturates, and metals have been shown to produce an increase in reactive oxygen species (ROS) in the liver. The authors examined the induction of oxidative stress by the organochlorine mouse hepatic carcinogen, dieldrin. Using a salicylate spin trap assay, dieldrin produced mouse liver-specific increases in ROS in cultured hepatocytes. Increased amts. of hepatic 8-hydroxy-2'-deoxyguanosine and malondialdehyde (MDA) and decreased levels of cellular antioxidants were also seen in cultured mouse hepatocytes following dieldrin treatment. In subchronically dieldrin-treated mice and rats, hepatic vitamin E (Vit E) decrease was correlated with the dieldrin dose. While Vit E levels were decreased in both rats and mice, the normal lower levels of Vit E in the mouse resulted in a subsequent oxidative stress, evidenced by an increase in MDA formation in the mouse liver. Dieldrin also produced a dose-dependent increase in DNA synthesis in the mouse (not the rat) following subchronic treatment. These effects seen in both cells in culture and in vivo were species-specific, organ-specific, and dose-dependent which directly correlated with the observed pattern of cancer induction for dieldrin in rodents (mouse liver-specific). These findings support a possible role for the induction of oxidative stress in nongenotoxic hepatic carcinogenesis possibly through modulation of gene expression.

L17 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:643357 CAPLUS
DOCUMENT NUMBER: 119:243357
ORIGINAL REFERENCE NO.: 119:43231a,43234a

TITLE: Hepatomegaly is an early biomarker for hepatocarcinogenesis induced by peroxisome proliferators

AUTHOR(S): Takagi, Atsuya; Sai, Kimie; Umemura, Takashi; Hasegawa, Ryuichi; Kurokawa, Yuji

CORPORATE SOURCE: Div. Toxicol., Natl. Inst. Hyg. Sci., Tokyo, 158, Japan

SOURCE: Journal of Environmental Pathology, Toxicology and Oncology (1992), 11(3), 145-9
CODEN: JEPOEC; ISSN: 0731-8898
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relationship between hepatomegaly and the hepatocarcinogenesis associated with by peroxisome proliferators was examined Male F-344 rats were maintained on diets containing clofibrate, ciprofibrate, nafenopin, gemfibrozil, Wy-14, 643, di(2-ethylhexyl) phthalate (DEHP), or di(2-ethylhexyl) adipate (DEHA) at carcinogenic doses for 1 wk. A close correlation between relative liver wts. and hepatocarcinogenicity was observed (r = 0.910). Administration of perfluorooctanoic acid (PFOA), perfluorodecanoic acid (PFDA), simfibrate or DL-040, for which hepatocarcinogenicity is not know, resulted in hepatomegaly in all treated

groups, this being especially marked in the PFOA case. Therefore, PFOA may have strong hepatocarcinogenic potential. Administration of the antioxidants BHA or vitamin E (VE) did not affect the hepatomegaly induced by DEHP. These results suggest that the hepatomegaly may be an early biomarker for prediction of the potential hepatocarcinogenicity of peroxisome proliferators. However, this requires further clarification in terms of its relation to the oxidative stress thought to be involved in peroxisome proliferator-induced hepatocarcinogenesis.

L17 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:207629 CAPLUS
DOCUMENT NUMBER: 116:207629
ORIGINAL REFERENCE NO.: 116:34959a,34962a
TITLE: Effects of the peroxisome proliferators ciprofibrate and perfluorodecanoic acid on hepatic cellular antioxidants and lipid peroxidation in rats
AUTHOR(S): Glauert, Howard P.; Srinivasan, Suseela; Tatum, Vickie L.; Chen, Li Chuan; Saxon, Danita M.; Lay, L. Travis; Borges, Tim; Baker, Michael; Chen, Linda H.; et al.
CORPORATE SOURCE: Dep. Nutr. Food Sci., Univ. Kentucky, Lexington, KY, 40506, USA
SOURCE: Biochemical Pharmacology (1992), 43(6), 1353-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to determine if hepatic cellular antioxidants and indexes of oxidative damage are altered by administration of the peroxisome proliferators ciprofibrate and perfluorodecanoic acid (PFDA). Rats were fed 0.01% ciprofibrate in the diet or were injected with PFDA (0.5 or 5.0 mg/kg, i.p.) every 4 wk for 6, 14, 30, 54, and 78 wk. Peroxisomal fatty acyl-CoA oxidase and catalase activities were increased by both ciprofibrate and PFDA throughout the study. Neither ciprofibrate nor PFDA increased the levels of malonaldehyde or conjugated dienes, but ciprofibrate decreased these indexes at early time points. Ciprofibrate decreased the following cellular antioxidants or antioxidant enzymes: vitamin C, vitamin D, DT-diaphorase, glutathione peroxidase, glutathione-S-transferase, and glutathione reductase; superoxide dismutase and glutathione were not affected. PFDA decreased DT-diaphorase and increased superoxide dismutase, but did not affect other cellular antioxidants. This study shows that administration of the peroxisome proliferators ciprofibrate and PFDA did not increase indexes of lipid peroxidn., but that cellular antioxidant defenses were inhibited for a prolonged period of time by the peroxisome proliferator ciprofibrate.

L17 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:167903 CAPLUS
DOCUMENT NUMBER: 110:167903
ORIGINAL REFERENCE NO.: 110:27729a,27732a
TITLE: Relationship of oxidative damage to the hepatocarcinogenicity of the peroxisome proliferators bis(2-ethylhexyl) phthalate and Wy-14,643
AUTHOR(S): Conway, James G.; Tomaszewski, Konrad E.; Olson, Michael J.; Cattley, Russell C.; Marsman, Daniel S.; Popp, James A.
CORPORATE SOURCE: Chem. Ind. Inst. Toxicol., Natl. Inst. Environ. Health

Sci., Research Triangle Park, NC, 27709, USA
SOURCE: Carcinogenesis (1989), 10(3), 513-19
CODEN: CRNGDP; ISSN: 0143-3334
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Wy 14,643 at 0.1% in the diet produced a much higher incidence of hepatic cancer in male rats than 1.2% DEHP in the diet. Both diets, however, caused similar degrees of peroxisome proliferation. To investigate this difference in carcinogenicity, H2O2-detoxification mechanisms and indexes of oxidative damage were evaluated in male rats fed 1.2% DEHP or 0.1% Wy 14,643 for up to one year. DEHP or Wy 14,643 treatment increased hepatic catalase activity .apprx.25% from 8 to 365 days. DEHP or Wy 14,643 treatment decreased hepatic glutathione peroxidase activity by 50% from 8 to 365 days. Glutathione concns. were not affected by 151 days of DEHP or Wy 14,643 feeding. The similar effects of DEHP and Wy on H2O2 detoxification enzymes and glutathione concns. suggests that these factors are not responsible for the widely different carcinogenicities of Wy 14,643 and DEHP. Hepatic vitamin E concns. were 50% lower in rats receiving Wy 14,643 for 151 days as compared to rats fed DEHP or control diets. Lipofuscin, which was contained within lysosomes, was increased 3-fold after 39 days of DEHP and remained at this level up to 365 days of treatment. In comparison, lipofuscin was increased 4-fold after 18 days of Wy 14,643 and continued to accumulate in a linear manner reaching values 30-fold over controls after 365 days of treatment. DEHP treatment for 39-365 days increased the activities of the lysosomal enzymes α-fucosidase, β-galactosidase, and N-acetylglucosaminidase 50-100%. The same enzyme activities were increased .apprx.4-fold after 39-365 days of Wy 14,643. Lysosomal cathepsin B activity was unchanged by DEHP but doubled by 151 and 365 days of Wy 14,643. Acid phosphatase activity was unchanged by DEHP but increased by 50% after 151 and 365 days of Wy 14,643. In addition, conjugated dienes were increased (.apprx.45%) only in rats receiving Wy 14,643 for 151 and 365 days. These data show for the first time that the magnitude and time course of lipofuscin deposition, induction of lysosomal enzymes and conjugated diene accumulation, is correlated closely with the degree of carcinogenicity. Wy 14,643-induced decreases in hepatic vitamin E concns. could contribute to the observed accumulation of conjugated dienes at later time ponts. The data suggest that lipofuscin accumulation is an early biomarker that is quant. predictive of the carcinogenicity of the peroxisome proliferators DEHP and Wy 14,643.

L17 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:149597 CAPLUS
DOCUMENT NUMBER: 110:149597
ORIGINAL REFERENCE NO.: 110:24621a,24624a
TITLE: Nafenopin, a peroxisome proliferator, depletes hepatic vitamin E content and elevates plasma oxidized glutathione levels in rats
AUTHOR(S): Lake, Brian G.; Gray, Tim J. B.; Korosi, Sally A.; Walters, David G.
CORPORATE SOURCE: Br. Ind. Biol. Res. Assoc., Carshalton/Surrey, SM5 4DS, UK
SOURCE: Toxicology Letters (1989), 45(2-3), 221-9
CODEN: TOLED5; ISSN: 0378-4274
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Male Sprague-Dawley rats were given oral doses of nafenopin (80 mg/kg/d) for up to 28 d. Nafenopin administration resulted in liver enlargement and induction of peroxisomal fatty acid β-oxidation enzymes (which generate hydrogen peroxide), but little effect was observed on catalase, and cytosolic GSH peroxidase was decreased. Hepatic vitamin

E levels were depleted to .apprx.50% of control. A small increase in hepatic GSSG content was paralleled in a time-dependent increase in plasma GSSG. The changes in vitamin E and GSSG levels may represent early indicators of oxidative stress produced in rat hepatocytes by nafenopin and other peroxisome proliferators as a consequence of the increased production of hydrogen peroxide.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	339.21	347.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-76.00	-76.00